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THE NOMENCLATURE OF THE FILARIA OF THE PACIFIC PRODUCING NON-PERIODIC EMBRYOS (*WUCHERERIA PACIFICA*).

By Sir Philip MANSON-BAHR, C.M.G., D.S.O., M.D., F.R.C.P.

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It is therefore now open to question whether morphological distinctions in adult filarial nematodes are of themselves sufficiently valid in the zoological sense as a mark of specificity. Pathological effects, peculiar geographical distribution, and selective capacity for insect intermediaries may henceforth be considered to be of determinative value. This criterion now applies apparently to what has so far been regarded as the non-periodic form of *Wuchereria bancrofti*. The adult forms of the non-periodic filaria which were obtained by the writer in Fiji are indistinguishable, on morphological grounds, according to Prof. R. T. LEIPER, from those of the type species—*Wuchereria bancrofti*—with nocturnal periodic embryos. This feature was at that time (1912) employed as an argument in favour of its identity with this type, but in view of these recent developments, other characteristics appear to be sufficiently valid for recognition of specific status to yet a third species of Wuchereria in man, for which the name *Wuchereria pacifica* is now proposed, and of which the intermediary mosquito host is *Aëdes variegatus* (Doleschall, 1858).*

* Formerly known as *Stegomyia pseudoscutellaris* Theo. 1910.

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The non-periodic character of the Pacific microfilaria was first described by V. G. THORPE (1896) from specimens collected in Tonga and Fiji. He found, to his astonishment, that the embryos occurred in large numbers in the blood, both by day and by night. Subsequently, in Fiji, G. W. A. LYNCH (1905), A. D. BRUNWIN (1909) and B. M. WILSON (1909) drew attention to the same phenomenon, as well as to the apparent identity of the microfilariae with those of *W. bancrofti*. This again was abundantly confirmed by the writer (1912) and, as already stated, the parental stages proved to be identical with those of the classical type, and there is now no reasonable doubt from re-examination of the original specimens that the microfilaria is identical with that of the periodic *W. bancrofti*. From the contiguous island of Samoa non-periodic microfilariae were demonstrated in Hamburg by F. FÜLLEBORN (1912), who showed conclusively that, in some natives from that island who were visiting Germany, this lack of periodicity was entirely unconnected with the waking or sleeping habits of the human host, as had been suggested by MANSON. This subject was also fully investigated by LEBER and v. PROWAZEK (1911) in Samoa itself.

Similar microfilariae were found in the Wallis Islands by BROCHARD (1910), in Tahiti by DUBRUEL (1909), in the southern Cook Islands (Rarotonga and Aitutakai) by A. MCKENZIE (1925), by S. LAMBERT (1926), and by G. H. E. HOPKINS in Tongatabu, Haapai, and Vavau of the Tonga group (*see* BUXTON, 1928). According to A. BREINL (1915) there may also be localities in S. New Guinea where the non-periodic microfilaria also occurs. F. W. O'CONNOR (1923) found it abundant in the Ellice and Tokelau Islands, in the latter of which *Aëdes variegatus* is the only mosquito known. According to LAMBERT (1924) this form of filariasis is known in the S. Gilbert Islands, where, however, an extensive survey has not so far been made. According to P. A. BUXTON it is known to be present in the Society Islands, and in the whole of Polynesia, but, on the other hand, the nocturnal periodic *W. bancrofti* prevails in Melanesia and Micronesia, the Bismarck Archipelago, New Caledonia, Solomon Islands and New Hebrides. Buxton has indicated that in an eastward direction this nocturnal form is limited by the longitude of 170°E, but that further than that the filaria is non-periodic.

In 1906, P. M. ASHBURN and C. F. CRAIG described a single case in the Bilibid prison in Manila of a non-periodic microfilaria which they named (on its embryonic characteristics) *Filaria philippinensis*. Subsequently E. L. WALKER (1914) found four other examples, but on examining adult filariae extracted from Filipinos identified them as morphologically similar to *W. bancrofti*. According to J. M. PHALEN and H. J. NICHOLS (1909) the nocturnal periodic microfilaria is the most widespread variety in the Philippines: the non-periodic being quite exceptional. However, in view of recent developments, I have re-examined the photomicrographs which illustrate Ashburn and Craig's paper and it is possible that, from the specific characteristics which they depict, they may have been describing *Microfilaria malayi*, in which the periodicity, for some reason or other, may have been disturbed. At any rate, at this distance of time, this is a most difficult question to settle as the embryos were in such small numbers in the bloodstream that it was difficult to determine fluctuations in numbers. It has not been possible to find out whether, under laboratory conditions, *W. malayi* can develop in *Culex fatigans*. The comparative

tightness of the sheath at the posterior end of the microfilaria and the arrangement of the nuclei at the head resemble *Microfilaria malayi*. Some reasonable doubt may therefore be entertained whether this Philippine non-periodic microfilaria is indeed identical with the Pacific form.

As an attempt to explain the non-periodic character of the Fijian filaria I originally suggested (1912) that this feature was an adaptation to the habits of the mosquito intermediary in the Pacific—*Aëdes variegatus*—which is a day-biting species. Since that time it has been firmly established (Buxton) that this is the only efficient intermediary in the whole of the Pacific area, whilst he and O'Connor have shown too, that in many of the smaller atolls (such as the Tokelau group) it is the only species of mosquito to be found, and further that, whilst other species such as the night-biting *Culex fatigans* and *Aëdes aegypti* are importations, *A. variegatus* must be regarded as an original inhabitant of the Polynesian islands. It is significant too, in this respect that O'Connor found the microfilaria rate in the Ellice Islands to be in direct relationship to the prevalence of *A. variegatus*. In Nukulalai, or Mitchell Island, where conditions are unfavourable to this mosquito, the filarial incidence is the lowest in the group.

P. A. Buxton in his great work in the Pacific (1928) has advanced the theory that a gradual conversion from nocturnal to non-periodicity took place; it being assumed that the nocturnal microfilaria was brought by the original immigrant Polynesians who came from S.E. Asia into the Pacific. Here people left a country rich in mosquitoes for one in which remarkably few occur, as there are only six indigenous species in the whole of Polynesia. *Aëdes variegatus* never bites at night, but most avidly in the early morning and towards dark at a time when only a few microfilariae are present in the blood of a nocturna-infected individual just prior to the midnight swarm. The mosquitoes (*A. variegatus*) thus gradually became infected and the filaria, previously nocturnal in habit, then became non-periodic and adapted to this particular mosquito as its normal intermediary. It appeared to Buxton's sense of reasoning that in this manner the mystery of the non-periodicity of the microfilaria in Polynesia could be most satisfactorily explained. But one may add that if that adaptation were so perfect why did not the periodicity become entirely diurnal?

The range of the non-periodic Polynesia filaria is, as far as is at present known, coextensive with that of *Aëdes variegatus* (and its varieties) with the possible exception of the Philippine non-periodic filaria described by Ashburn & Craig to which reference has already been made.

There are, however, still some disquieting facts which should temper judgment. Buxton has established that *Aëdes variegatus* is present in the Bismarck Archipelago, Solomon Islands and New Hebrides where the nocturnal microfilaria abounds, though it is possible that future research may indicate that both forms, nocturnal and non-periodic, are present in this area, just as *W. malayi* and *W. bancrofti* are in Ceylon and Malaya. He gives a table showing that :—

Aëdes variegatus var. *tongae* occurs in Tonga.

A. v. hebrideus in the New Hebrides.

A. v. pseudoscutellaris in Fiji, Samoa, Cook Islands, Society Islands, Marquesas, Tokelau, and Paumotu Groups.

The adaptation of the non-periodic microfilaria to *Aëdes variegatus* is so complete, as was demonstrated by the writer in Fiji, that development

to full capacity takes place in that insect to an extent not previously known in the transmission of the nocturnal microfilaria in the night-feeding *Culex fatigans*. Now we learn that the historic vector of nocturnal filariasis, *Culex fatigans* (BUXTON & HOPKINS 1927) is a recent introduction into Polynesia and is still to be found principally in harbour towns and foreign settlements, but not in the more remote islands. In Fiji the writer was able to show that the non-periodic Polynesian microfilaria does not develop readily in this mosquito any more than it does in the second imported species—*Aëdes aegypti*.

Most significantly too O'Connor in 1920 in the most heavily infected island—Funafuti—did not find a single example of *Culex fatigans*, out of a large number dissected, infected with this filaria under natural conditions. In other words, neither of these insects is an optimum host for the parasite.

But here we are presented with a difficulty in the complete understanding of this puzzling problem because it was shown that *Aëdes variegatus* is a satisfactory host for the nocturnally periodic filaria of those Indians and Solomon Islanders who had recently arrived in Fiji. It would appear justifiable from this evidence to assume: (1) that the adaptation of this filaria to *Culex fatigans* has been lost from long-standing lack of opportunity, or (2) that such an adaptation has never in fact existed. The latter seems to offer an additional and reasonable basis for regarding the non-periodic microfilaria as a species distinct in the biological sense.

We are faced with some additional facts about which some adequate explanation must be offered. I was able to prove that, in immigrants who normally harbour the nocturnal form and who had been long resident in Fiji, the non-periodic microfilaria alone could be demonstrated. The assumption here would seem to be: (1) that the original nocturnal periodicity had been disturbed as the result of adaptation to a new intermediary—*Aëdes variegatus*—a hypothesis which is assuming intelligent foresight on the part of a lowly nematode parasite as suggested by Buxton, or (2) that these natives had become infected with the local species of filaria during their residence in Fiji.*

This riddle can be finally and definitely solved solely by continuous observation, under controlled conditions, of a nocturna-infected individual in Polynesia over a considerable number of years, but the second assumption appears at present to be more likely because the writer found absolute *nocturnal* periodicity in two Solomon Islanders who had resided in Fiji ten years.

Therefore periodicity is not lost by residence and intimate contact with *A. variegatus*. *Per contra*, I found nothing but the non-periodic microfilaria in Europeans, long resident in Fiji, who had contracted their infection there, and also in other immigrant races such as Indians and Melanesians who had been born and bred in the islands or who had been in the islands since their youth.

Other important aspects of this question lie in the pathological effects produced by the non-periodic filaria and whether these considerations can influence final judgment. That the Pacific filaria is the main agent in the production of elephantiasis there can be no reasonable doubt. There are, however, some other suggestive features: Elephantiasis of the arms is more common in the Pacific, as I have

* See also statement by H. H. SCOTT (A History of Tropical Medicine, Vol. II, p. 1069) wherein the same point of view is ably expressed.

shown, than in other areas where typical *W. bancrofti* is common, so also, as Buxton remarks, is elephantiasis of the breasts. The very considerable glandular enlargements which are associated with the Polynesian filaria have arrested the attention of many observers. The writer originally noted hypertrophy of the epitrochlear glands in infected Fijians and this has been abundantly confirmed by O'Connor, Buxton and others. Enlargement of these glands is not commonly associated with *W. bancrofti* filariasis in other parts of the world, but such a generalization cannot be considered to be complete in view of the fact that Buxton found quite a proportion of New Hebrideans infected with nocturnal filariae to have enlarged and palpable epitrochlears. Another remarkable feature of non-periodic filariasis is the rarity of chyluria and lymphuria in Polynesia. My experience led me to believe that these phenomena are extremely rare in Fiji and they are, according to Buxton, very exceptional in Samoa, though A. F. MACKAY (1927) recorded one interesting case in that island. Chyluria, on the other hand, is of comparatively frequent occurrence in nocturnal periodic *W. bancrofti* infections in Egypt, India, the West Indies and in S. America.

We see from this brief statement that non-periodic filariasis presents some distinctive clinical features as in the somewhat parallel case of *W. malayi* filariasis. To these peculiarities may be added the large number of non-periodic microfilariae which are found in the blood-stream in the absence of any physical signs of disease.

Assembling all these factors, and in the light of recent developments of our knowledge of this genus of Filariae, I believe that the recognition of the Polynesian filaria as a separate species in the biological sense would best fit all the hitherto known facts and the name *Wuchereria pacifica* is now proposed as being most descriptive of the filaria in the Pacific and its adaptation to *Aëdes variegatus*—an insect indigenous to this area.

It may be argued that *W. pacifica* is not a well established species in the sense that *W. bancrofti* and *W. malayi* may be considered to be. The probability is that it is a species in the process of evolution and represents the primitive filaria of the Polynesian which on account of its geographical position has become isolated in the zoological sense and biologically adapted to its surroundings, but whether it is the more primitive form of *Wuchereria* and the nocturnal periodicity a subsequent development is a matter for future investigation. The periodic or non-periodic habit of microfilariae in the blood stream has received recognition from systematists in assessing specific characters as in the well-known cases of *Loa loa* and *Acanthocheilonema perstans*. If this conception is correct then the fact of the lack of filarial periodicity in Indian and Solomon Islanders long resident in Fiji, who have thus become infected during their sojourn with the non-periodic local species *W. pacifica* becomes more intelligible.

It is regretted that, so far from simplifying the problem underlying the mechanism of filarial periodicity, this exposition has rendered it even more complex. In the present state of knowledge we cannot say more than that periodicity is a primary principle ramifying throughout the whole of Nature. We see it in the periodic cycles of intracorpuscular plasmodia, in the migration of birds and fishes, the swarming of bees, the efflorescence of flowers and in many other ways. Periodicity is an inherent quality and as such is distinctive to a species as is any structural feature.

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SUMMARY OF RECENT ABSTRACTS.*

VI. PLAGUE.

Epidemiology and Epizoology.

HAMPTON (p. 822) gives the history of plague in the United States. Since its introduction there have been 499 cases in eight States, but sylvatic plague is widespread in the west, and many rodents have been found infected. Fleas, lice and ticks from these rodents have been shown to harbour the bacilli.

MACCHIAVELLO (p. 424) has studied the epidemiology of plague in Chile. It has been characterized by acute outbreaks followed in successive years by outbreaks of decreasing intensity until, in some localities, it has completely disappeared. But this cycle has been repeated time after time, and the author considers that it is not a question of recrudescence from the rat reservoir, but a reintroduction from abroad—for instance of plague fleas in bales of jute from India—starting an epizootic which leads to human disease. In Chile the same author (p. 425) reports on the results of rat examinations. In 88 rats from which the bacilli were isolated, 5 had acute disease, 64 were in chronic or subacute stages and 19 showed no lesions. This indicates the presence of healthy rat carriers and the author draws the conclusion that the total rat population of places in which plague has broken out should be destroyed. In a village in the State of Rio de Janeiro, PINOTTI *et al.* (p. 824) describe a small outbreak which was preceded by an epizootic in rats. This was regarded, not as an exacerbation of enzootic disease, but as a new importation from Rio de Janeiro.

In the province of Chimborazo, Ecuador, SUÁREZ (p. 423) reports an outbreak of 16 cases of pneumonic plague. The area is sparsely populated and he states that both the rat and the flea ordinarily concerned in the spread of plague are not present. Plague, however, is endemic, with epidemic outbreaks in which some of the cases present throat symptoms. The author has found plague bacilli in throat

* The information from which this series of summaries has been compiled is given in the abstracts made by the Sectional Editors in the *Tropical Diseases Bulletin*, 1940, Vol. 37. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

smears of several persons in contact with cases of plague and has confirmed their identity by culture and animal inoculation. He believes that such latent cases may account for outbreaks by man to man transmission, and that prophylactic measures should include search for, and treatment of, human carriers. [It would be instructive to know for how long these bacilli remained in the throats of contacts.] DE LA BARRERA (p. 423) reports an outbreak in the Mendoza province of the Argentine, where sylvatic plague is present. In this instance a human case of septicaemic plague terminated in pneumonia and was followed by eight other cases of direct infection. [It would seem possible that this course of events might explain the outbreaks described by SUÁREZ above, though he does not mention sylvatic plague.]

Two foci of plague are reported from the Belgian Congo, one in the region of Butembo to the west of Lake Edward (VAN HOOF, p. 419), the other near Lake Kivu (VAN RIEL and MOL, p. 419). The latter probably belongs to the group of places on the borders of the Congo, Uganda, Kenya and Tanganyika, in which plague is endemic. DEVIGNAT (p. 828) describes his method of inoculating guineapigs subcutaneously with marrow aspirated from the bones of captured rats. By this means the plague area round Lake Albert (Belgian Congo) has been defined. *Mastomys ugandae* is the domestic rat of this region, and 287,962 of these rodents were dealt with in this fashion. In some places apparently healthy rats were found to be infected [see also Macchiavello above]. VAN HOOF (p. 419) reports that in the Belgian Congo *P. pestis* has been isolated from rodents of the genera Mastomys, Leggada, Agricanthis, Lemiscomys, Lophuromys. VAN RIEL and MOL (p. 419) state that *Mastomys ugandae* and *Rattus rattus alexandrinus* are carriers in the Kivu area of the same country.

LAMBORN (p. 824) reports a small outbreak in a village near Blantyre, Nyasaland, which had been preceded by a mild enzootic in field rodents.

GIRARD (p. 829) records rat plague, in a district of Madagascar, which has persisted for 12 years and has given rise to occasional cases in man.

ROSIER (p. 425) gives the incidence of plague in Java in 1938 as 2,107 cases ; although the epidemic (which is diminishing) is essentially one of bubonic disease, there were 202 cases of primary pneumonic plague, of which 48 occurred in one outbreak.

MEYER (p. 424) reports that Wyoming and New Mexico have recently shown plague infection of wild rodents, and states that it has once more been found that the inoculation of guineapigs with pooled fleas, lice and ticks has yielded more information than the examination of shot or trapped rodents. MILLER (p. 823) writes of the possible spread of sylvatic plague from the United States to Canada, and states that already an infected gopher, *Citellus r. richardsonii* has been found in Alberta.

SÁENZ VERA (p. 824) considers that in S. Ecuador plague is endemic in field rodents and that there is a link between these rodents and man. This link is probably the cui, a small rodent of the hamster type [the name is used for *Microcavia australis* and *Graomys griseoflavus*]. Human plague is here a rural disease and does not occur in epidemics. This is probably due to the fact that the rat population inhabits fields where food is abundant, and there is no need for field rodents to resort to inhabited centres for food. In the *Boletin Sanitario*, Buenos Aires (p. 424) it is stated that extensive sylvatic plague has been found in the Province of Salta, Argentine ; the rodent concerned was of the genus

Sylvilagus. Man may be infected directly from these rodents, but more usually the domestic rat becomes infected through its habit of feeding on dead animals, and passes the disease to man. De la Barrera (p. 423) in the Mendoza Province of the Argentine shows that *P. pestis* has been isolated from cuis of the genera Microcavia and Galea, *Graomys griseoflavus*, *Mus musculus* and *Lepus europaeus*. The original infection of wild rodents probably came from domestic rats.

Yokoyama (p. 427) reports that in Manchuria ground squirrels of the genus Citellus are numerous and play the chief part in the transmission of plague. Black rats are rare and the Tarabagan is not found.

Transmission.

Rao (p. 418) discusses *Xenopsylla astia*, a notoriously inefficient vector of plague, though capable of transmitting it experimentally. He thinks that one reason why it is inefficient in nature is probably that it is highly susceptible to adverse climatic conditions, especially high temperature and low humidity.

van Hoof (p. 419) reports that *P. pestis* was found, in the Belgian Congo near Lake Albert, in fleas of various species: *Xenopsylla brasiliensis*, *X. cheopis*, *Ctenocephalus canis*, Sarcopsylla and Ctenophthalmus. There is another small focus near Lake Edward, but *X. cheopis* is not present, and this may account for the limited spread there.

De la Barrera (p. 423) states that Parapsyllus and Rhopallopsyllus, fleas of wild rodents in the Argentine, have been shown capable of transmitting plague to man.

Aetiology.

Rao (p. 826) defines a bacterial growth factor as a substance without which no growth will take place. There are two main types: simpler molecules such as the amino acids, and more complex molecules like thiamin and nicotinic acid. Only three amino acids are indispensable to *P. pestis*: proline, phenylalanine and cystin, and the complex factors are not indispensable but have a stimulatory action on metabolism and growth. Several growth factors or coenzymes were tested for stimulatory activity. Haematin, cozymase, thiamin and nicotinic acid all stimulate the respiration of *P. pestis*. These may be essential components of the bacillus, synthesized in the course of growth.

Sokhey (p. 825) has shown that *P. pestis* is definitely a capsulated organism, and that the capsule is present whether the strain is virulent or avirulent. The envelope (which is distinct from the capsule) appears to be nothing more than a peculiar settling down of the fine particles of India ink at a distance from the capsule, due to the operation of physical forces [this view does not appear to accord with that of Bhatnagar, this *Bulletin*, 1941, Vol. 38, p. 328, who finds some correlation between the amount of envelope substance and virulence and protective power]. Wats *et al.* (p. 827) have studied envelope material, and while they consider that the soluble substance (envelope material) obtained from washings of growth is not dependent on the production of smooth or rough colonies, yet a rough strain tends to be poor in this soluble substance. They state, however, that there

is no relation between this soluble substance and virulence, but that the titre of the substance seems to indicate the antigenic value of a strain.

Wats & Puduval (p. 827) have obtained two types of colony on blood agar, one smooth and translucent from a virulent strain, the other rough and irregular from an avirulent strain. There were no differences in carbohydrate and protein reactions, but in broth the smooth strain gave uniform turbidity and the rough gave a granular deposit.

Rao (p. 825) has measured the oxidative activity of *P. pestis* in culture towards hexoses, pentoses, organic acids and amino acids, finding the activity to be in that order, *i.e.* the highest towards the hexoses. This activity is closely correlated with fermentation activity. Glucose and lactose are the best and cheapest sources of carbon for media; the useful amino acids are named. Russo (p. 422) has studied the fermentation reactions of *P. pestis*, especially those of freshly isolated strains, which differ in some respects from those of stock laboratory cultures. Details are given.

Wats *et al.* (p. 420) have found certain serological differences between *P. pestis* grown at 28°C. and those cultivated at 37°C. With bacilli grown at 28°C., agglutination by specific serum was slow, the flakes were small and the sediment compact. With bacilli grown at 37°C. agglutination was rapid, the flakes were large and the sediment voluminous. The 37°C. growth absorbs all agglutinins from sera obtained by immunizing animals with either 37° or 28° growths, but the 28° growth will only absorb its own agglutinins. The 37° growth, when heated at 100°C. for one hour, behaves like the 28° growth. The method of immunizing animals with these growths, for which the technique is not simple, is described.

Girard (p. 422) does not consider that the production of nitrite in liver bouillon is enough to distinguish *P. pestis* from other organisms. He regards the rhamnose test as much more absolute, stating that *P. pestis* does not ferment rhamnose, whereas *P. pseudotuberculosis* does [but Russo (above) states that most of his freshly isolated strains of *P. pestis* fermented rhamnose].

Savino *et al.* (p. 422) have isolated Pasteurella organisms from bone marrow cultures of rats in the Argentine. These were not *P. pestis*, and it is therefore concluded that it is not safe to diagnose plague in rats without putting the organism isolated to a complete cultural test for *P. pestis*.

Clinical Findings and Treatment.

Lewillon *et al.* (p. 828) describe a case of apparently primary plague meningitis.

Sokhey and Dikshit (p. 828) quote experiments with mice which indicate that sulphathiazole is much superior to sulphapyridine in treatment, both before and after the septicaemic state has set in. Even in septicaemia a dose of 40 mgm. sulphathiazole given twice daily for 10 days cures 80–90 per cent. of the animals. As plague is much more severe in the mouse than in man there seems to be a prospect of a great advance in therapy by means of this compound. Sulphanilamide therapy is referred to by van Hoof (p. 419). Moreau (p. 829) reports recovery in two patients with bubonic plague treated by E.V. serum and the sulphonamide preparation Bacteramide.

Control.

Rosier (p. 425) refers to the house improvement scheme in Java, which is one of the principal anti-plague measures. In 1938, 56,265 houses were remodelled, bringing the total to 1,525,364, and 54,548 new houses were built on approved anti-plague lines. Soerono (p. 426) also writes of this house improvement scheme, describing the progress made in the Madja district of Java. This is a wealthy area and materials such as wood, bamboo and tiles are readily available. No compulsion was used other than strenuous propaganda, but it is noted that inspection and condemnation of houses, isolation of contacts and spleen puncture in suspected cases after death were unpopular. There were 8,070 houses due for improvement, and although the voluntary system was employed, all except 0·38 per cent. of these had been remodelled within 4 years. The only financial inducement given was a bonus of three florins for each completely reconditioned house. This great success of the voluntary system, which has been followed by the complete elimination of plague, is encouraging, though it is realized that progress cannot always be so good.

Sokhey *et al.* (p. 427) state that rat proofing of dwellings and the building of suitable grain godowns is not economically possible in India; poisoning and trapping of rats are not very successful, and the usual methods of dealing with fleas are even less so. Fumigation with HCN is effective but dangerous, but fumigation with the new proprietary cyanide compounds is now a practicable measure. Calcid briquettes are eminently satisfactory for fumigation. Ahluwalia (p. 830) points out that cyanide preparations are particularly useful because they kill not only rats but also fleas. Fumigants such as carbon monoxide or sulphur dioxide are less effective or less convenient. He has compared the efficiencies of Calcid and Cyanogas and reports in favour of the former. With proper control and under trained supervision he thinks that there is no danger in the use of Calcid in inhabited areas.

Paranjothy (p. 831) reports that in herd experiments with strains of Salmonella and Pasteurella and with Ectromelia, these organisms failed to precipitate epidemics in rat populations. They therefore appear to be ineffective anti-rat agents. He discusses the diseases carried by rats and has investigated certain commercial viruses and chemical poisons. Yokoyama (p. 427) has studied the infectivity of certain strains of Salmonella for ground squirrels and rats in Manchuria. Paranjothy (p. 831) reports on experiments with bacterial exotoxins, which proved to be of little value as rat poisons, and on various chemical poisons used in the Department of Agriculture. Danzel (p. 427) claims that Red Scilla (*Urginea scilla*) is lethal to the rat and the rat alone. The active principle is presumably a glucoside. In the report of the plague campaign in Hawaii (p. 830) are given instructions for the preparation of banana phosphorus bait.

Sáenz (p. 423) argues that if the guineapig rodents of Riobamba, Ecuador, are the main cause of epidemic outbreaks of plague, there is no other remedy than complete extermination. In the province of Loja, however, this author (p. 824) states that it would be almost impossible to exterminate the cuis which are the sylvatic reservoirs.

Junior (p. 832) discusses the work of the plague laboratory in São Paulo.

Vaccination.

With living organisms.—GIRARD (p. 829) in Madagascar argues that plague may persist in rats in rural areas for long periods, giving rise to occasional outbreaks in man. The destruction of fleas in native huts is impracticable, and the author concludes that efficient vaccination of the population is the best measure of protection.

GIRARD and RADAODY-RALAROSY (p. 830) report observations on the situation and persistence of the avirulent E.V. strain of *P. pestis* in the guineapig.

SAVINO and ANCHEZAR (p. 426) have tested the E.V. and Tjiwidej (Otten) strains of attenuated *P. pestis* for their immunizing power in guineapigs. Both appear to cause a mortality of about 30 per cent. of the animals, but the remainder show solid immunity against virulent infection. Both strains give rise to subcutaneous nodules, whereas avirulent but non-immunizing strains do not; the authors consider the E.V. strain to be superior to the Tjiwidej in immunizing power.

In Java, ROSIER (p. 425) reports that in the period 1935 and 1938, almost 7½ million vaccinations with the living vaccine of Otten have been performed.

With dead organisms.—SOKHEY (p. 420) has made careful and extensive investigations into the preparation of vaccines. He shows that nutrient agar is not the most suitable solid medium for the growth of *P. pestis*, and states that the medium of choice is blood agar and the optimum temperature 37°C. for this medium, though this temperature is very unfavourable for growth in fluid media. For the counting of viable organisms in broth cultures the author insists first on strictly standard conditions of growth, and the plating on blood agar in progressive tenth dilutions of standard quantities over standard areas. By this method of counting it has been found possible to devise a constant infective dose, and he gives details of the doses necessary to produce 100 per cent. fatality in white mice, house rats, white rats and guineapigs. Virulence is measured by finding the smallest number of organisms, cultivated at 25° to 27°C., which under standard conditions will kill all members of a batch of inbred white mice within 3 to 11 days; relative virulence could be further measured by taking the average period of survival. Maintenance of virulence in stored strains may be effected by incubating on blood agar at 26° to 32°C. for four days and then sealing and storing the tubes at 4° ± 2°C.

In the Belgian Congo VAN HOOF (p. 419) notes that most of the prophylactic vaccination is carried out with killed vaccines, since the living E.V. vaccine, which consists of an avirulent strain from Madagascar, is still regarded as on trial. *Charles Wilcocks.*

HELMINTHIASIS.

PRÉCIS OF ABSTRACTS IN THIS SECTION.

General.—MAPLESTONE and BHADURI (p. 374) give an account of the helminths of dogs in Calcutta, of which by far the most important is *Echinococcus granulosus.*

CHANG and LIN (p. 375) report on the intestinal parasites of man in Chengtu. Ascaris is the commonest worm; hookworm infection was found chiefly in soldiers, who had mostly been farmers before joining the army. YOUNG and HAM (p. 375) record the intestinal parasites found in a mental hospital in S. Carolina, and MEIRA and AMARAL (p. 375) the results of faecal examinations of labourers in Brazil.

VYAS *et al.* (p. 376) have described the preparation of synthetic anthelmintics.

Trematodes.—VERMOOTEN (p. 376) shows that schistosomiasis is present in collections of water, or in rivers, near Johannesburg, at Middleburg and at Pretoria. He points out that a final cystoscopic examination is necessary before a patient can be pronounced cured.

KRAKOWER (p. 376) gives the results of his investigations on the influence, of heat and cold, light, *p*H, salt and glucose on the longevity and activity of cercariae of *S. mansoni*,.

SCOTT (p. 377) shows that *S. mansoni* infection, which is common in Venezuela, is transmitted by *Australorbis glabratus* and that this snail occurs only in districts where there are irrigation canals. If the snails were prevented from breeding in these canals it is probable that they could scarcely maintain themselves elsewhere, and elimination of infection through snail control appears to be a definite possibility.

MEIRA (p. 378) considers that the Takata reaction will prove of little clinical significance in *S. mansoni* infection.

BRACKETT (p. 378) has examined sections of skin subjected to experimental infection with *Cercaria elvae* and *C. stagnicolae*. Burrows were found but there was no evidence that the cercariae had passed deeper than the Malpighian layer. There was invasion by eosinophils and acute inflammation. He notes that he has been exposed to schistosome cercariae many times and that on recent occasions the skin reaction has been more severe than was usual in the earlier exposures, and that almost immediate urticarial responses are now provoked. He (p. 379) has studied the biology of the snail hosts of *Cercaria stagnicolae* and *C. physellae*. Adult *Stagnicola emarginata* die out about August, and swimmers' itch begins then to disappear. *Physa parkeri* dies out earlier. CORT *et al.* (p. 379) regard the great increase in swimmers' itch in N. Michigan as due rather to more frequent use of bathing beaches than to increase in snail infection.

HSÜ and LI (p. 380) have proved experimentally that *Bithynia longicornis* is a first intermediate host of *Clonorchis sinensis*. It is abundant in fish ponds in the endemic area of Canton. They (p. 380) describe the migration of the larval stages of *C. sinensis* in *B. fuchsiana*.

CHU (p. 380) has found that the addition of certain dyes in certain strengths to the media in which *C. sinensis* were kept resulted in lengthening of their lives; weaker solutions were less effective.

TANG (p. 381) has compared the two types of *Paragonimus* (*P. ringeri* and the rodent type) in Fukien, South China. CHEN (p. 381) details the morphological appearances of *Paragonimus iloktsuenensis*, which cannot infect wild cats, pigs, guineapigs or monkeys. This fluke is found in the plains and is regarded as a valid species, as are *P. westermanii*, *P. kellicotti* and *P. ohirai*.

SANDGROUND (p. 382) has found a new species of Plagiorchis, *P. javensis*, in the small intestine of a Javanese.

MANSON-BAHR and WALTON (p. 382) describe a woman in England from whose common bile duct *Fasciola hepatica* was removed at operation. There were no eggs in the faeces and no eosinophilia. STIGLICH (p. 383) reports four cases of infection with *F. hepatica* in Peru. Eggs were found in the faeces of only one but were disclosed by duodenal sound in all. Emetine was useful in treatment.

SANDGROUND and BONNE (p. 383) report that tetrachlorethylene is rapidly effective in the treatment of infection with *Echinostoma lindoensis* [*sic*, but *lindoense* would appear to be grammatical] and describe morphological characters of the worm. Development takes place in the planorbid *Anisus* (*Gyraulus*) *sarasinorum* and metacercariae are found in other snails and mussels, the latter of which are part of the regular diet of the natives. LARIOS RODRIGUEZ (p. 383) reports five infections of man with *Echinostoma revolutum* in Mexico. In all the diagnosis was parasitic colitis with abdominal pain, diarrhoea and eosinophilia, and eggs were found in the stools. The intermediate hosts are *Limnaea attenuata*, *Physa osculans* and *Planorbis tenuis*. BEAVER (p. 384) describes investigations on the life history of the echinostome *Euparyphium melis*, the cercaria of which encysts in tadpoles and of which the snail *Stagnicola emarginata angulata* is an intermediate host. Adults have been found in the mink and other animals, and HSÜ (p. 384) reports that he has found two of the flukes in a man in Peiping. *C. W.*

MAPLESTONE (P. A.) & BHADURI (N. V.). **The Helminth Parasites of Dogs in Calcutta and their Bearing on Human Parasitology.**—*Indian Jl. Med. Res.* 1940. Oct. Vol. 28. No. 2. pp. 595–604. [27 refs.]

"1. Twenty-one different helminth parasites have been recovered from the 200 dogs examined by us. The complete list of worms found in dogs in India includes 50 species and of these 10 are now recorded by us in this paper for the first time.

"2. One of them *T. colubriformis*, which is a common parasite of herbivora and occasionally of man, has never before been found in a carnivore.

"3. No member of the genus *Paramphistomum* or of the family *Troglotrematidae* has ever before been recorded in dogs, and *P. sufrartyfex*, whose known distribution is limited to North-Eastern India, has hitherto been found in pigs several times and in man twice.

"4. The two flukes *H. heterophyes* and *O. felineus* are common parasites of man in other parts of the world, so they are important potential parasites of man in India. As both these worms depend on eating of raw fish for their transmission, the Indian is protected from acquiring them by the fact that he rarely indulges in this form of diet. The same set of circumstances also limits the incidence of *G. spinigerum* infection in human beings in India.

"5. By far the most important parasite of the dog in Calcutta as a menace to the health of man is *E. granulosus* the incidence of which is fairly high for city dogs.

"6. The absence of *T. ovis* from all our dogs, coupled with our failure to identify *C. ovis* in mutton sold in Calcutta, disposes of our previously held opinion that this tapeworm was a possible source of

at least some of the cases of human cysticercosis, of which an unduly large number has been seen in British troops in India during the past few years."

Chang (K.) & Lin (C. C.). **Intestinal Parasite Infections of Man in Chengtu and its Vicinity.**—*Chinese Med. Jl.* 1940. Nov. Vol. 58. No. 5. pp. 570–581. With 1 map. [13 refs.]

By means of two faecal smears, one in normal saline and one in iodine, 2,896 persons were examined. They were in four categories, namely 1,578 hospital patients mostly out-patients at the United University Hospital, 1,011 school-children, 241 soldiers and 66 inmates of a home for the aged, all in or near Chengtu.

A table gives the discovered incidences of seven protozoal and 11 helminthic infections. Among the latter Ascaris was by far the commonest, the percentage figures for the four groups being 36·76, 82·49, 68·89 and 57·58; hookworms were found in only one child, though the percentage in soldiers was 34·02; Trichuris was highest (19·7) in the aged. The rarer helminthic infections discovered were—Strongyloides one in a patient, *Toxocara canis* one in a child, *C. sinensis* three in patients and four in soldiers, *F. buskii* 10 in patients, *S. japonicum* two in patients, *T. saginata* one in a patient, both onchospheres and proglottids being seen, Taenia of unidentified species, four in patients.

In more detail the soldiers had mostly been farmers before going into the army, and had often gone barefoot or in straw sandals, facts falling in with their high hookworm incidence; for Ascaris another table shows reports of its incidence by various workers in China. Clonorchis seems hitherto not to have been reported from man in Szechuan Province though present in 35 per cent. of cats as the Provincial Bureau reports. Only one of the *F. buskii* hosts had even been outside the Province. One of the patients harbouring *S. japonicum* reported that persons with similar symptoms lived near him just outside Shwangliu city and a local survey of Oncomelania snails is being undertaken. It is believed that *A. lumbricoides* and *E. histolytica* have quite distinct modes of transmission in West China.

Clayton Lane.

Young (Martin D.) & Ham (Coyt). **The Incidence of Intestinal Parasites in a Selected Group at a Mental Hospital.**—*Jl. Parasitology.* 1941. Feb. Vol. 27. No. 1. pp. 71–74.

These infections were found in the faeces of 142 mental patients in South Carolina. Examinations were of material in simple saline and saline iodine. Percentages were: Parasites of all kinds 90, helminths 92, made up of Strongyloides 39, hookworm 66, Trichuris 78, Ascaris 10; protozoa 65 including Balantidium 5. *C. L.*

Meira (João Alves) & Amaral (A. Dacio F.). Considerações sôbre disseminação helmíntica entre operários, com especial referência aos casos positivos para *S. stercoralis* e *S. mansoni*. [**Incidence of Helminths among Labourers, especially of** *Strongyloides stercoralis* **and** *Schistosoma mansoni*.]—Reprinted from *Rev. Biol. e Hig.* São Paulo. 1940. June. Vol. 10. No. 2. pp. 119–138. [13 refs.]

The results of faecal examinations on labourers at São Caetano, Brazil.

Two series of examinations were made. One was of 297 persons, apparently as a routine measure, using concentration by sedimentation; the other comprised 105 who complained of digestive trouble and who were examined by smear and by Willis gravity floatation. The percentages of infections detected by the two methods were respectively: all helminthic infections 68·3 and 56·19, Necator 39·7 and 19·04, Ascaris 16·8 and 9·52, Trichuris 16·8 and 8·57, Enterobius 0·64 and 5·71, Strongyloides 1·6 and 19·04, *H. nana* 1·3 and 1·91, Taenia 0·64 and 0·995, *S. mansoni* 5·05 and 09·95.

[Between the two series there are two known variables—different techniques and the absence or presence of digestive trouble. From these data conclusions as to the effects of these variables on the deposit or detection of eggs may not safely be drawn.] *C. L.*

Vyas (V. A.), Bokil (K. V.) & Nargund (K. S.). **Synthetical Anthelmintics, Part I: α-Substituted-γ-Butyrolactones.**—*Jl. Univ. Bombay.* 1940. Nov. Vol. 9. N.S. Pt. 3. pp. 145–149.

Rosenmond and Schapiro [*Arch. Pharm.*, 1934, Vol. 271, p. 315] concluded that "a butyro-lactone structure is essential for the development of anthelmintic properties" and that the lactone must be attached to a benzene nucleus with hydroxy or methoxy group as a substituent. The authors describe the method of preparation of several such bodies. *C. L.*

Vermooten (Vincent). **Bilharzia as seen by the Urologist.**—*Proc. Transvaal Mine Med. Officers' Assoc.* 1940. Aug. Vol. 20. No. 221. pp. 11–14.

Medical men and the public in S. Africa pay too little attention to schistosomiasis, and a broadcast address has stated that those on the Reef at 5,000 feet altitude do not stand risk of infection. That is not so. Thus the Yokeskei river just outside Johannesburg is infected, and so are the Brakpan and other collections of water on the Reef. Again, Cawston has reported that in Middleburg, situated only 30 feet below the supposedly critical altitude, half the children are infected, while in Pretoria, only 350 feet lower, nearly a third are so. With water cooler by night than by day, night instead of day bathing may lessen infection. After a general survey of the illness, it is stressed that there must be certainty that treatment has effected cure and for that there must be a final cystoscopic examination. Surgical treatment has been disappointing so long as infection has been active. In answer to a comment in the discussion the author noted that he had seen only one case of rectal infection, which, however, was half an inch outside his territory. *C. L.*

Krakower (Cecil A.). **Some Observations of the Effects of Physical and Chemical Agents on the Cercariae of** *Schistosoma mansoni*.—*Puerto Rico Jl. Public Health & Trop. Med.* 1940. Sept. Vol. 16. No. 1. pp. 26–44. [Spanish version pp. 45–65.]

The agents considered are temperature, light of various sorts, *p*H, and common salt and other solutions.

The investigation started from the accidental observation that when normal saline was added to the rain water, in which the snails

had been put for the collection of cercariae, these dropped to and remained at the bottom of the container. The technique consisted in obtaining an even heavily charged suspension of cercariae and maintaining its evenness when chemicals were added ; for its examination test tubes were found far better than watch glasses. In rain water the normal cercarial life span was 24 to 48 hours, a few living to 72 hours, and any stimulus caused those that were alive and active to ascend in a cloud to the surface. Freezing was rapidly fatal, but at a temperature of 5° to 6°C. they became motionless and dropped to the bottom, yet most lived for 4 to 6 days and a few for 12 or 13. When, after being at this temperature for 4 days they were activated by warmth, infection could still be produced ; after longer than this in the cold obvious infection could no longer be found, though a few adults were identified in the liver of a rat after cercariae used for infection had been in the cold for 8 days. At temperatures up to 34°C. they lived as long as at room temperature, above this temperature mortality increased, and all were killed after 8½ hours at 40°C., most after 2 hours at 42°C., about three-quarters after 15 minutes at 44°C., and all after 30 minutes at 45°C.

Darkness did not shorten life ; strong electric light from 200 watt bulbs did, the induced activity apparently wearing them out ; ultra-violet light killed all after 45 minutes ; direct sunlight killed, but whether this was due to light or to heat was unsettled. A *p*H of 4·6 to 10 left them unaffected, that of 3 and 11 killed. Sodium chloride solution of 1·5 per cent. killed the cercariae quickly, one of glucose of 2·7 per cent. injured them ; the effects of a stay in isotonic solutions of these for not more than 8 hours passed off when the cercariae were put in rain water. There is a report on the effects of other solutions and it is pointed out that the cercaricidal and lytic effects of rabbit serum for cercariae can be demonstrated *in vitro*.

C. L.

Scott (J. Allen). **Schistosomiasis in Venezuela.** [Paper read at 16th Ann. Meeting of American Society of Parasitologists. Abstract taken from *Supp. to Jl. Parasitology*. 1940. Dec. Vol. 26. No. 6. pp. 23–24.]

" There are probably somewhere in the neighbourhood of 30,000 persons in Venezuela infected with *Schistosoma mansoni*. The infection is practically coextensive with the distribution of the transmitting snail, *Australorbis glabratus*, and occurs only in districts where irrigation is in use. It is not present in all such districts, nor are the snails found exclusively in irrigation water. Nevertheless, it seems probable that if the snails were prevented from breeding in the irrigation systems, they could scarcely maintain themselves elsewhere. The infection is principally found in valleys of the mountain range which extends along the central part of the northern coast. In the east the few foci reported are apparently small and local. West of the basin of Lake Valencia the infection is not found because the intermediate host is replaced in the fauna by *Tropicorbis* sp., while in the higher mountains farther west no planorbid snail is common in the steeper valleys. Our examinations do not cover the great plains south of the mountains nor the regions beyond the Orinoco, but it seems certain that any foci in these areas must be extremely local. The prevalence of infection is somewhat variable but in many

regions over 90 per cent. of the males above 10 years of age are infected, while the proportion of females infected is usually slightly lower. Virtual elimination of the infection through snail control seems a definite possibility requiring only money and perseverance." [See also this *Bulletin*, 1940, Vol. 37, p. 484.]

MEIRA (João Alves). Sôbre a reação de Takata na esquistosomiase mansonica. [**Takata Reaction in Mansonian Schistosomiasis.**]—Reprinted from *Rev. de Med.* São Paulo. 1940. Sept. Vol. 24. No. 81. pp. 44–60. With 3 figs. [17 refs.] English summary.

Probably the Takata reaction will prove of little clinical significance in Mansonian schistosomiasis.

The study is of 23 patients. In two of them a piece of liver removed during a splenectomy showed marked cirrhosis, and the reaction was positive in one and negative in the other. In eight of them the reaction was negative before anthiomaline treatment began, afterwards it remained so in seven but became positive in one. In two in whom the reaction was positive the albumin-globulin ratio in the serum was studied; albumin was lessened and the normal ratio might be reversed.

C. L.

JANER (José L.). **Miracidial Twinning in** *Schistosoma mansoni*. [Research Notes.]—*Jl. Parasitology*. 1941. Feb. Vol. 27. No. 1. p. 93.

A "Siamese twin" formed by two miracidia joined together for the anterior two-thirds of their length and lying within an eggshell of normal size. *C. L.*

CAWSTON (F. Gordon). **Characteristics of the Freshwater Mollusc found in Southern Rhodesia and the Union of South Africa and Popularly Known as** *Physopsis africana* **Krauss.**—*Jl. Trop. Med. & Hyg.* 1940. Nov. 15. Vol. 43. No. 22. pp. 262–264. With 1 fig. [10 refs.]

BRACKETT (Sterling). **Pathology of Schistosome Dermatitis.**—*Arch. Dermat. & Syph.* 1940. Sept. Vol. 42. No. 3. pp. 410–418. With 3 figs.

The skin of the inner aspect of the forearm was deliberately infected with *Cercaria elvae* and *C. stagnicolae*, affected parts were excised after an interval, were fixed, and were serially sectioned and stained with haematoxylin and eosin.

The area excised 50 hours after infection with *C. elvae* measured 2·5 by 1 cm., that excised 29 hours after infection with *C. stagnicolae* was near the last but about twice its size. No cercariae were found in the tissues in either, but in both there were burrows in the epithelium and evidence of acute inflammation. As to the 29-hour-old lesions :—

"These burrows were traced from section to section and in several cases from a point where they entered on the surface to a place where they ended blindly, still within the malpighian layer. No evidence was seen which indicated that the cercariae had gone beyond this layer into the deeper tissues. For the most part the lesions were almost completely filled with neutrophils, which in places formed intraepithelial abscesses. Generalized edema in the vicinity of the burrows and in the cutis and the subcutaneous tissue below them was pronounced. Lymph vessels were

dilated and easily seen." In the 56 hours old lesions "The burrows were still confined to the epithelial layer, and in following some of them from section to section there was seen no evidence that the cercariae had penetrated into the deeper tissues. The channels were filled in places with loosely arranged debris and with some recognizable neutrophils and lymphocytes. In other places the burrows were completely empty or showed evidence of having contained a more or less clear fluid. Above some of the burrows were edematous infiltrations between the malpighian layer and the cornified tissue. The acute inflammatory reaction seemed to have subsided considerably, but, in contrast to the picture in the earlier sections, a striking invasion of eosinophils had occurred. The latter cells were present in large numbers in the subcutaneous and dermal tissues and formed a large percentage of the cells that could be identified within the lumens of the burrows and in the superficial edematous patches. . . . I have been exposed to schistosome cercariae both experimentally and naturally many times each summer since about 1934 and each year my reaction has been increasingly pronounced. At the outset the lesions were mild and caused little trouble, but by the time the biopsies were made in 1938 and 1939, penetrating cercariae would cause an almost immediate urticarial response. Within half an hour the area of penetration would be swollen, and often within 12 hours inflamed lymph vessels could be traced for more than half the length of the forearm."

It is pointed out that some people show no reaction after contact with these cercariae probably, it is suggested, because they do not enter the skin. *C. L.*

Brackett (Sterling). **Studies on Schistosome Dermatitis. VIII. Notes on the Biology of the Snail Hosts of Schistosome Cercariae in Wisconsin and Epidemiological Evidence for the Life Cycles of Some Avian Schistosomes.**—*Amer. Jl. Hyg.* 1940. Nov. Vol. 32. No. 3. Sect. D. pp. 85–104. [21 refs.]

The cercariae dealt with are *Cercaria stagnicolae* and *C. physellae* whose respective intermediate hosts are *Stagnicola emarginata* and *Physa parkeri*. The biology of these snails is here correlated with the seasonal prevalence of swimmer's itch.

The life span of these snails is never much more than a year, the adults usually die soon after breeding, and the young hatch about the same time so that after the death of the adults all snails are of about the same age. When the itch is caused by penetration of *C. stagnicolae* the adult snails from which they have emerged (*S. emarginata*) die about August and swimmer's itch then begins to disappear; when it is by *Ph. parkeri* it ceases earlier, for the snails die earlier in the year. Evidence suggests that *C. physellae* is the larval stage of *Pseudobilharziella querquedulae* of the blue-winged teal. *C. L.*

Cort (W. W.), McMullen (D. B.), Olivier (Louis) & Brackett (Sterling). **Studies on Schistosome Dermatitis. VII. Seasonal Incidence of *Cercaria stagnicolae* Talbot, 1936, in Relation to the Life Cycle of its Snail Host, *Stagnicola emarginata angulata* (Sowerby).**—*Amer. Jl. Hyg.* 1940. Sept. Vol. 32. No. 2. Sect. D. pp. 33–69. With 1 map & 8 graphs. [22 refs.]

This covers in detail much of the other paper with this practical point:—

"The great increase in the prevalence of schistosome dermatitis in the last 10 years in northern Michigan is probably due to the increase in the use

of the beaches for bathing purposes rather than to any increase in infection of the snails with the schistosome cercaria. Without active control measures it seems certain that the incidence of this dermatitis will continue to increase with the increase of the summer tourist business which will lead to a constant development of new beaches for swimming purposes."

C. L.

Hsü (H. F.) & Li (S. Y.). **Studies on Certain Problems of *Clonorchis sinensis*. VIII. Experimental Proof of *Bithynia longicornis* as the First Intermediate Host of *C. sinensis*.**—*Chinese Med. Jl.* 1940. Mar. Supp. 3. pp. 241–243.

The evidence given is that 200 *Bithynia longicornis* collected near Peiping were fed on Clonorchis eggs washed from the gall bladder of a cat. They developed cercariae with the morphology of those of *Clonorchis sinensis*. Into an aquarium were put 180 of these snails and certain laboratory bred *Pseudorasbora parva*, and the latter developed cysts identical with those of *C. sinensis*. The flesh from these infected fish was given to laboratory bred cat and guineapig, and the adult flukes were found in the bile tracts of both animals. *B. longicornis* is abundant in the fish ponds in the Canton area, which is an endemic centre of clonorchiasis. *C. L.*

Hsü (H. F.) & Li (S. Y.). **Studies on Certain Problems of *Clonorchis sinensis*. IX. The Migration Route of its Early Larval Stages in the Snail, *Bithynia fuchsiana*.**—*Chinese Med. Jl.* 1940. Mar. Supp. 3. pp. 244–254. With 36 figs. on 10 plates.

When *B. fuchsiana* swallows Clonorchis eggs, the miracidia hatch out either in rectum or intestine, become sporocysts in the wall of the organ concerned, and the sporocysts migrate into surrounding lymph spaces, or into those surrounding stomach, oesophagus or even liver. There they produce rediae which migrate into these spaces within the liver and other parts including foot and mantle. *C. L.*

Chu (H. J.). **Studies on *Clonorchis sinensis* in Vitro. Part III. Survival Period in Relation to Certain Dyes.**—*Chinese Med. Jl.* 1940. Mar. Supp. 3. pp. 255–259.

When trypan blue, methyl green or acid fuchsin in the strengths shown below were added to the medium in which *C. sinensis* was kept *in vitro* the life of the flukes was lengthened.

In methyl green solution, 1 in 5,000, the flukes lived up to 135 days, in trypan blue solution, 1 in 2,500, up to 51 days, in acid fuchsin the lengthening of life was slight. A weak solution is not so effective in prolonging life. *C. L.*

Chu (H. J.) & Hsü (Chien-liang). **Studies on *Clonorchis sinensis* in Vitro. Part IV. Combined Effect of Gentian Violet and X-Rays.**—*Chinese Med. Jl.* 1940. Mar. Supp. 3. pp. 260–266.

A combination of very weak gentian violet with comparatively low X-ray dosage shortened the life of Clonorchis *in vitro*. *C. L.*

Tang (C. C.). **A Comparative Study of Two Types of Paragonimus occurring in Fukien, South China.**—*Chinese Med. Jl.* 1940. Mar. Supp. 3. pp. 267–291. With 23 figs. on 6 plates. [27 refs.]

Two types of Paragonimus are, it is believed, present in the Fukien Province, their distribution overlapping in the Foochow-Futsing region. They are designated the *ringeri* type and the rodent type.

The *ringeri* type redia averages about twice as big as that of the rodent type, namely length of 1·21 mm. as compared to 0·56 mm., and breadth of 0·35 compared to 0·15, the method of preparation being the same in each group. The cercaria of the rodent type has long spines on the postero-lateral parts of the body, that of the *ringeri* type has not. The metacercaria of the *ringeri* type in crabs has a very thick cyst wall averaging 0·014 mm. in depth, that of the rodent type is membranous. Perhaps these mean specific differences. Of the *ringeri* type the first larval host in Fukien is *Melania toucheana* and the second *Potamon* (*P.*) *denticulatus*. The corresponding animals in the rodent type are *Katayama tangi* and *Parathelphusa* (*P.*) *sinensis*. The need is urged for investigation of such differences in India and the Philippines. *C. L.*

Chen (H. T.). **Morphological and Developmental Studies of *Paragonimus iloktsuenensis* with Some Remarks on Other Species of the Genus (Trematoda : Troglotrematidae).**—*Lingnan Sci. Jl.* 1940. Oct. 26. Vol. 19. No. 4. pp. 429–530. With 134 figs., 1 chart & 14 plates. [61 refs.]

"The present work covers a detailed study of the morphology of the adult of *Paragonimus iloktsuenensis* Chen, its life history and its comparison with certain species of the genus of which material is on hand. The parasite so far is found naturally only in rats.

"A detailed historical account of the occurrence of the genus in China from the aspect of geographical distribution is given. The review shows that detailed life history is known only to this species in this country.

"Morphological studies of the adult indicate that the present species is very similar to other species except for cuticular spines. The latter are variable in shape, but are typically elongated, broad at base and tapering gradually to the tip. The base may be square or rounded, or may be occasionally divided lengthwise. The tip may be pointed, bluntly pointed or bluntly pointed with serrated edge, or as broad as, or broader than, the base or broad with serrated edges. In arrangement the spines may be in rows, or in clusters or occasionally singly spaced. The spines on the ventral side between the two suckers are in groups of two (rarely one) to as many as five or six with two to four being the commonest, and on the ventral side between the two testes in groups of from two to about ten with five or six being the commonest.

"Other adult structures which appear to have diagnostic values are the more delicate branchings of the ovary, the more slender central mass of the testes, the larger size of the seminal receptacle, and the curved manner of the seminal vesicle.

"The metacercaria is an oval body with one wall only. It is very thin and easily broken. This distinguishes the present species from

all other members of which the life histories are known. Definite differences are also encountered in eggs and second generation rediae. Little can be said regarding other stages until more data from other species are available.

"Based on experimental feedings it has been found that *P. iloktsuenensis* cannot infect wild cats, pigs, guineapigs and monkeys. When compared with known records it indicates that host specificity may be an important factor in distinguishing this species from others.

"By basing on the habitat of the intermediate hosts of various species of *Paragonimus* it is possible to divide the species of which the life history is known into 'plain breeders' and 'hilly breeders.' Of the former *P. iloktsuenensis* is a representative and of the latter *P. westermani*.

"As a result of the present studies it may be tentatively concluded that *P. westermani*, *P. kellicotti*, *P. ohirai* and the present species are valid species. The status of *P. compactus* requires further investigation as no material is available for comparison although it appears to be a good species on the basis of Vever's description."

SANDGROUND (J. H.). *Plagiorchis javensis* **n. sp. A New Trematode Parasitic in Man.**—*Rev. Med. Trop. y Parasit.* Habana. 1940. July–Aug. Vol. 6. No. 4. pp. 207–211. With 1 fig.

The third reported instance of a Plagiorchis species parasitizing man. The first record was by AFRICA and GARCIA [*Papers on Helminthology: 30th Jubileum of the Activities of K. J. Skrjabin.* Moscow. p. 9] who found five specimens in the small intestine of a native of the Province Ilocos Sur, Philippines; the second was when MCMULLEN [*Jl. Parasitology*, 1937, Vol. 23, p. 113] deliberately infected himself and various local birds, and identified the flukes as *P. muris* Tanabe, 1922. This third instance came to light while the contents of the small intestine of a Javanese were being sieved in the Pathological Institute at Batavia. One worm only was found there. It measured under 2 mm. long and under 1 mm. wide and looked like a small fleshy barley grain. It is described and illustrated and will be deposited in the Helminthological Collection of the U.S. National Museum, Washington. The worms that Africa and Garcia left unnamed, to avoid the unnecessary multiplication of doubtful species, Sandground names *P. philippinensis*, holding that to name a parasite eases indexing and helps later workers. *C. L.*

MANSON-BAHR (Philip) & WALTON (James). **The Surgical Removal of *Fasciola hepatica* from the Common Bile Duct with a Commentary upon this Infection in Man.**—*Brit. Jl. Surgery.* 1941. Jan. Vol. 28. No. 111. pp. 380–383. [14 refs.]

F. hepatica was removed from the bile duct of a woman of 54. She had never been outside the British Isles, was fond of watercress, and chewing grass when on a country walk. At 18 years old she had a tapeworm, at 29 biliary colic with passage of gallstones, at 39 the colic returned, at 46 she had it again and the gall-bladder was removed and had small calculi in its wall but none in its lumen. At 53, after reappearance of the pain, pancreatitis was suspected and on laparotomy the common bile duct was found dilated, was opened, and the parasite was disclosed and removed. It measured 23 by 13 mm. It is noted

that outside the liver there were no evidences of infection—no eggs in the faeces and no marked eosinophilia—and it is pointed out that among obscure cases of hepatic disease, other such infections may have been missed, and that it seems to be the second instance in which removal of this parasite from the bile duct of man has been reported.

C. L.

Stiglich (Germán). **Distomatosis hepática.**—*Rev. Méd. Peruana.* 1940. Sept. Vol. 12. No. 141. pp. 311–322.

A description from Lima, Peru, of four cases of infection with *Fasciola hepatica.*

Epigastric colic and icteric tinge over the sclera were present, the eggs of the parasite disclosed by the duodenal sound in all, but found in the faeces in one only, though *E. histolytica* was present in three and hookworm eggs in one, while in one there was eosinophilia up to 25 per cent. Emetine hydrochloride was valuable in treatment. *C. L.*

Sandground (J. H.) & Bonne (C.). *Echinostoma lindoensis* **N. Sp., a New Parasite of Man in the Celebes with an Account of its Life History and Epidemiology.**—*Amer. Jl. Trop. Med.* 1940. July. Vol. 20. No. 4. pp. 511–535. With 2 plates. [13 refs.]

So far as it adds to the authors' earlier paper [this *Bulletin*, 1940, Vol. 37, p. 491] their summary of this one runs thus :—

" The parasites are rapidly expelled by tetrachlorethylene medication and as many as 250 worms have been recovered after a single treatment. The species is characterized by the possession of 37 collar spines ; in this respect it resembles *Echinostoma revolutum* Froelich more than it does any other member of the Echinostomidae recorded from man. While the morphological features whereby the marita stage may be distinguished from that of *E. revolutum* are not striking, it appears that more tangible differences may be recognized in the redia and cercaria stages. At Lake Lindoe larval development was found in natural infections of a small planorbid, *Anisus* (*Gyraulus*) *sarasinorum* ; the metacercaria was found in several pulmonate snails, e.g., *Viviparus javanicus rudipellis* and also in the mussel, *Corbicula lindoensis* Boll., which occurs in large numbers in certain parts of the lake. These mussels form a regular part of the diet and the echinostome infection rates in the 3 villages are proportionate to the distances that the villagers have to travel to procure mussels for the pot and, by the same token, to pollute the lake so as to bring about infection of the mussels.

" Infection of man with the production of the characteristic worms followed the ingestion of mussels. Rats and mice have also been experimentally infected, but the worms do not grow as large as they do in man and the worms are spontaneously expelled a few weeks after attaining maturity."

Larios Rodriguez (Ignacio). *Echinostoma revolutum* (Froelich, 1802), (Trematoda : *Echinostomidae*) estudiado por primera vez en México como parásito del hombre. [Thesis.] [*E. revolutum* **studied for the First Time in Mexico as a Parasite of Man.**]—82 pp. With 40 figs. [17 refs.] 1940. Mexico, D.F.

A general consideration of *E. revolutum*, and a description of five infections in man, one of them experimental.

In all the diagnosis was parasitic colitis, eggs having been found in the stools with, in the natural infections, Ascaris twice, Enterobius

twice, *H. nana* and *T. solium* once, both in the same patient. Hexylresorcinol was effective in unworming. The experimental infection was in a medical student, aged 22, who swallowed 20 cysts in a capsule, and 11 days later had intense abdominal pain lasting for 24 hours, and diarrhoea with pale yellow stools containing some scybala, and an eosinophilia of 15·5 per cent. In the natural infections this ran as high as 24 per cent. with haemoglobin down to 70 per cent. The intermediate hosts—*Limnaea attenuata, Physa osculans* and *Planorbis tenuis*—are described and pictured and experimental infections have been obtained in duck and pigeon by feeding cysts from the hepatopancreas of these snails, and it is evidently these that were used for the human infection. *C. L.*

i. Beaver (Paul C.). **Studies on the Life History of *Euparyphium melis* (Trematoda : Echinostomidae).**—*Jl. Parasitology.* 1941. Feb. Vol. 27. No. 1. pp. 35–44. With 13 figs. on 1 plate. [12 refs.]

ii. Hsü (H. F.). ***Euparyphium jassyense* Leon and Ciurea (= *E. melis* (Schrank)) found at the Autopsy of a Chinese.**—*Chinese Med. Jl.* 1940. Nov. Vol. 58. No. 5. pp. 552–555. With 3 figs. on 1 plate.

i. An echinostome cercaria was found in 1 of 133 adult *Stagnicola emarginata angulata* which seemed to be identical with *Euparyphium melis* (Schrank, 1788). Next year 1 of 550 of these snails was found infected with the same parasite, of which the redia, cercaria, metacercaria and adult are now described.

When the cercariae are placed in a vessel with tadpoles they rapidly enter the cloacae of these, penetrate its wall and encyst in skin or subcutaneous tissue. In three weeks they are probably infective. A ferret was fed on 5 tadpoles, representing about 100 metacercariae 26 to 37 days old, got diarrhoea and was killed on the eleventh day in case the illness should expel adult parasites. High up in its duodenum one fluke was found and in its stomach a quantity of towelling of which it had eaten 30 square inches and which perhaps caused its upset. No note on the ferret's antecedents has been found in the paper. Though the fluke was immature its structure sufficed for positive identification, and it and an average sized specimen from a mink are fully pictured.

ii. At autopsy two trematodes were found in the small intestine of a Chinese male who had died in the Peiping Medical College Hospital of chronic myelogenous leucaemia. They are described and are identified in the terms set out in the title. But Szidat (1940) has recently pointed out that *E. jassyense* as described by Léon and Ciurea [see this *Bulletin*, 1922, Vol. 19, p. 651] is identical with *E. melis* of badgers, hedgehogs and other mammals in Europe and of dogs in Japan ; moreover, one of Hsü's two specimens happens to agree with the outstretched specimens of *E. melis* described by Szidat, and the other with *E. jassyense* as figured by Leon and Ciurea, so the latter name becomes a synonym of the former [and lapses under the Code of Zoological Nomenclature]. The patient had left Peiping for Jehol, but a few months later started back and being too poor for other means of travel walked back. This took four months during which he

weakened, for he suffered from dysentery and ate irregularly, and he died six days after entering hospital. It is suggested that he may have swallowed tadpoles on his journey. *C. L.*

SPRUE.

Précis of Abstracts in this Section.

Manson-Bahr (p. 386) writes of the value of nicotinic acid in the treatment of the glossitis of pellagra and sprue, and of riboflavin in angular stomatitis. The glossitis of pernicious anaemia also responds to nicotinic acid, and the author refers to other points of similarity between this disease and sprue, idiopathic steatorrhoea and pellagra. He then reports a series of cases of sprue treated with nicotinic acid, noting its curative effect not only on the glossitis, but also on the gastrointestinal symptoms and the skin. For haemopoiesis liver therapy is necessary. The author distinguishes between non-tropical sprue and idiopathic steatorrhoea ; the former is the analogue, in temperate climates, of tropical sprue. Tecoz (p. 388) describes a case of early sprue in which there were symptoms resembling those of pellagra. Treatment with nicotinic acid and a liver preparation produced improvement.

de Langen (p. 388) found that the flat curves of blood fat and blood sugar in sprue were improved after the administration of liver extract, especially the impure preparations.

Hanes and Reiser (p. 389) discuss the relation of phosphorus to fat and glucose metabolism in sprue. The observed delayed fall in serum phosphorus after glucose ingestion indicates that the sugar reaches the blood stream slowly and is there as slowly absorbed. The findings indicate the slow rate of intestinal absorption in sprue. Erf and Rhoads (p. 389) quote investigations which suggest that, in sprue and pernicious anaemia, glycine is more slowly absorbed than in normal persons from the gastrointestinal tract. After the administration of liver extract this abnormality was not found. Chitre and Patwardhan (p. 390) have studied the absorption of calcium from the duodenum of anaesthetized dogs.

Mackie and Mills (p. 390) describe changes in the X-ray appearances of the small intestine in sprue, idiopathic steatorrhoea and chronic ulcerative colitis with deficiency disease.

Markoff (p. 391) discusses the aetiology of non-tropical sprue and describes the case of a patient in whom the condition developed after resection of 1·5 metres of small intestine. He considers that local inflammatory changes in the ileum may lead to sprue symptoms and that mild gastroenteritis may be the starting point. Non-tropical sprue is a clinical syndrome and the main location of the disease process is the whole length of the small intestine.

Allen (p. 392) reports a case of non-tropical sprue in which there was a tendency towards severe haemorrhage, which was to some

extent remedied by administration of vitamin K. There is probably, in sprue, a defective absorption of the vitamin which leads to deficiency of prothrombin in the plasma.

CHILDS and DICK (p. 393) record a case of non-tropical sprue in which the administration of pancreatic juice brought about a more definite improvement in the stools than did liver extract alone. The findings recorded by the authors suggest that there is a deficiency in some as yet undemonstrated pancreatic factor. The use of dried pancreatic substance apparently caused improvement in the appetite and in the blood condition.

O'SULLIVAN (p. 394) describes two cases of idiopathic steatorrhoea in adults. In comment MOORE remarks that the fundamental fault is usually imperfect absorption from the small intestine, especially of lipoid material, resulting from chronic jejuno-ileal insufficiency.

C. W.

MANSON-BAHR (Philip). **The Treatment of Sprue with Vitamin B_2 and its Bearing upon the Aetiology of this Disease.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1941. Mar. 27. Vol. 34. No. 5. pp. 347–372. With 1 chart. [117 refs.]

The introductory portion of this paper is concerned with a recapitulation of views previously expressed. [See this *Bulletin*, 1941, Vol. 38, p. 7.] The action of nicotinic acid upon pellagrous glossitis and the allied glossitis of sprue suggests that these two conditions are closely allied. The special action of riboflavin appears to be to heal the excoriations or the angular stomatitis which are frequently associated with sprue as well as with pellagra. This therapeutic effect indicates that pellagrous stomatitis is due to a vitamin B_2 deficiency and this may also be responsible for the conditions described by WILLIAMS, GILLAN and TROWELL as "pellagroid." Attention is drawn to the resemblance between these and the state generally recognized in general medicine as the Plummer-Vinson syndrome which is also characterized by glossitis.

The relationship between sprue and pernicious anaemia is next discussed. There appears to be some indication that the glossitis of this anaemia is closely allied to, if not identical with, that of sprue, and responds to nicotinic acid therapy. The differential diagnosis is not always easily established—the achlorhydria and hypochlorhydria which characterize pernicious anaemia do not always furnish a reliable index, because they are not uncommon in sprue. A table illustrates this point in which it is shown that achylia, achlorhydria, normal acid curve and hyperchlorhydria have been noted in sprue; there appears to be no connexion between the constitution of the gastric juice, glossitis, degree of anaemia, bilirubinaemia, blood calcium and essential progress of the disease. Therefore, in sprue, the acidity of the gastric juice cannot be correlated with absence of the intrinsic factor. A significant feature pointed out by JACOBSON is that anti-anaemic activity of the alimentary canal corresponds with the distribution of argentaffine cells. In pernicious anaemia they are absent and are said to be deficient also in sprue.

The geographical distribution of pernicious anaemia in relation to that of tropical sprue deserves some consideration. The facts appear to be that the former is extremely rare, if not entirely absent, in tropical native races. It may well be that pernicious anaemia, like

sprue itself, Cooley's anaemia and sickle-cell anaemia, may exhibit a distinct racial incidence, for sprue is also very seldom seen in pigmented native races.

A table of differential diagnosis illustrates the main points between pernicious anaemia, tropical sprue, idiopathic steatorrhoea and pellagra, wherein it is emphasized that the third named is, like pernicious anaemia, mostly a disease of the northern hemisphere. In the clinical pathology and associated anaemia there are many points of resemblance between these various clinical states.

The main portion of the paper is devoted to the treatment of sprue with nicotinic acid. A series of 24 well marked cases has been given therapeutic doses of nicotinic acid and 7 have received riboflavin in addition. The results are summarized in a table which sets forth the effect of nicotinic acid on sprue glossitis, part of which is the rapid return of taste-sense. It is claimed that the subsidence of these irritating symptoms exerts a profound influence upon digestion and assimilation. The fiery redness of the tongue in advanced sprue tends to fade under nicotinic acid therapy within 24 hours and its appearance is restored to normal within four days. In the glossitis of advanced sprue with marginal indentations and angular stomatitis the addition of riboflavin appears to be necessary. The dosage of nicotinic acid ranged in different cases from 150–300 mgm. a day and that of riboflavin was about 3 mgm. Probably further experience will suggest that larger doses than these are advisable.

The effect of the treatment upon the gastro-intestinal tract has been less easy to gauge. Usually diarrhoea ceases within 4 days and the stools become normal in size and colour within a period of 2–3 weeks. It has been possible under this treatment to permit a greater range and variety of diet than was formerly considered advisable; all have been able to resume active life and occupation. In one of the most advanced cases, with very severe anaemia, the patient returned to Ceylon and remained well. Flatulence and meteorism were strikingly absent from the series, a table is given of details. It is emphasized that nicotinic acid therapy must be prolonged for three, and intermittently thereafter for six, months.

It is not claimed that vitamin B_2 treatment exerts any influence upon haemopoiesis, and consequently it is necessary to persist with intensive parenteral liver therapy. Nicotinic acid has an effect upon the skin of advanced sprue, a rapid improvement takes place in appearance and texture coincident with increase in body weight. It is too early yet to assess the value of this treatment in preventing future relapses. The specificity of nicotinic acid treatment can be used in the recognition of allied states, such a one is "non-tropical sprue" which was well described by THAYSEN in 1932, and should be regarded as the analogue of tropical sprue in northern countries—distinct from idiopathic steatorrhoea and coeliac disease. Such a case was detailed by the reviewer in 1929 [see this *Bulletin*, 1930, Vol. 27, p. 346] and now two further examples are described, which have originated in London and in which response to nicotinic acid therapy has been as marked as in the classical disease. In the second case the increase in weight, whilst maintaining the same dietary, is illustrated by a graph.

It is concluded that, on the analogy with pellagra in which the typical uncomplicated disease is mainly tropical or subtropical in distribution on account of dietetic reasons, it is possible to postulate

that, though the sprue syndrome is commonly met with in its most highly developed form in tropical residents, yet manifestations of the same process may be encountered elsewhere, where it is recognized as "non-tropical sprue." *P. Manson-Bahr.*

TECOZ (R. M.). Stéatorrhée (genre sprue) avec symptômes pellagroïdes. [**Sprue-like Steatorrhoea with Pellagroid Symptoms.**]—*Rev. Méd. Suisse Romande.* 1940. Nov. 25. Vol. 60. No. 13. pp. 1040–1044. With 2 figs.

A plasterer, aged 43, came to hospital on account of digestive troubles, diarrhoea and frequent vomiting. He was observed to present a reddish-brown pigmentation of face, neck and fore-arms, unexposed parts not being affected. The skin of the hands was thickened, hard, and in places desquamating. The abdomen was swelled, tympanitic, slightly tender. The stools, 2–3 daily, were pasty, of butyric odour, not very large and not yeasty. Needles of fatty acids were abundant. Blood showed 4,100,000 r.b.cs., 6,500 white corpuscles per cmm., haemoglobin 80 per cent.; red cell diameter 6–7·5μ. No free HCl in the gastric juice, even after histamine. The blood sugar curve was low.

The pigmentation had appeared 18 years before, the digestive disturbances five years later. For ten years he had been on a strict diet of milk or tea and sugar, white bread and butter for breakfast; semolina or rice and milk at midday and once or twice a week a little minced veal. He was limited or limited himself to this meagre diet—one deficient in vitamins B_1, B_2 and C. He had frequent occipital headache and always felt cold.

His diet was improved, but changes were badly tolerated; he was given pepsin and hydrochloric acid, two injections of *Héparglandol* Roche and, thrice daily for 10 days, nicotinic acid. The general condition improved; vomiting was much less, fatty acids disappeared from the stools, but the pigmentation remained unaffected. The case appeared to be one of pellagra with commingled symptoms of early sprue. *H. H. S.*

DE LANGEN (C. D.). Het verloop der bloedvetcurve bij spruw. [**The Blood-Fat Curve in Sprue.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1940. Oct. 8. Vol. 80. No. 41. pp. 2391–2399. With 6 charts.

As a result of estimations carried out on sprue patients, before and after treatment, Professor de Langen has found that sprue patients after taking fat in the form of butter show a flat and usually a low level curve of blood-fat; in place of the normal rise of 50–80 per cent. in sprue the increase is never above 20 per cent. A similar flattened curve is seen after a glucose test. In both cases there is disturbance of absorption from the small intestine. When liver extract is administered parenterally the curve tends to approach the normal, and the "impure" preparations are more active in this respect than are the purified products. Treatment with nicotinic acid has a varying affect on the blood-fat curve, while cortine brings about no improvement.

H. H. S.

HANES (Frederic M.) & REISER (Raymond). **The Relation of Phosphorus to Fat and Glucose Metabolism in Sprue.**—*Amer. Jl. Med. Sci.* 1940. Nov. Vol. 200. No. 5. pp. 661–664. With 1 chart. [23 refs.]

The study was directed to obtaining evidence, or refutation, for the theory of VERZÀR that the underlying physiological defect in sprue is a breakdown in the phosphorylating mechanism of absorption.

The normal phosphorus changes in sprue after intravenous injection of glucose, and the close parallel between the degree of elevation of the respiratory quotient and blood sugar after glucose has been taken by the mouth can be taken as evidence that the patient is capable of metabolizing glucose normally, after it is in the blood. Consequently the delayed fall in the serum phosphorus after glucose ingestion can be explained solely on the basis that the sugar reaches the blood-stream very slowly and is then as slowly absorbed. This does not support the theory of THAYSEN that the low blood sugar curve is due to abnormally rapid assimilation of the absorbed glucose by starved tissues.

Similarly the delayed fall in respiratory quotient and the corresponding slight increase in blood fats and the failure of any serum phosphorus response after oil ingestion run parallel to conditions after glucose ingestion and make it evident that abnormal phosphorus changes result from the failure of the metabolite to reach the blood at a normal rate. Sprue patients do not exhibit the normal fasting diurnal variation in phosphorus excretion and, after ingestion of olive oil, there is an increase in urinary phosphorus excretion, whereas there is a decrease in normal persons, but there is no significant change in serum inorganic phosphorus.

These findings, as well as the delayed changes in respiratory quotient after oil and glucose meals, indicate the slow rate of intestinal absorption in sprue. *P. M.-B.*

ERF (L. A.) & RHOADS (C. P.). **The Glycine Tolerance Test in Sprue and Pernicious Anemia.**—*Jl. Clinical Investigation.* 1940. Mar. Vol. 19. No. 2. pp. 409–421. With 7 figs. [14 refs.]

FAIRLEY, BARKER and Rhoads, by sugar and fat tolerance recordings, have shown that absorption of these substances is improved after treatment of sprue patients with liver extract, and GROEN has similarly observed increased rate of glucose absorption by the intestinal tract in three cases of pernicious anaemia after similar therapy.

From these observations the conclusion was reached that, in both sprue and pernicious anaemia, dysfunction of the intestinal tract could be corrected by some constituent of liver extract, but so far no evidence has been advanced that it is also poorly absorbed when given by the oral route.

Accordingly studies have been made on the absorption of an amino acid—glycine—by sprue and pernicious anaemia patients, as well as those suffering from other disorders, such as ulcerative colitis, other varieties of anaemia and hepatic cirrhosis.

The *glycine tolerance test* was effected by the oral administration of 25 gm. of glycine dissolved in 500 cc. of water to the fasting patient at 9 a.m. Blood samples were withdrawn before the amino acid ingestion, and subsequently at hourly intervals till 3 p.m. Urine was collected in two series over the whole of the six hours of the test.

Plasma amino nitrogen, plasma and urinary urea nitrogen levels were determined by the method of van Slyke.

In four patients with untreated sprue and pernicious anaemia the results of glycine tolerance tests suggested that glycine was more slowly absorbed from the gastrointestinal tract than normal, but evidence of this abnormality was not found in the same cases after the administration of liver extract.

A similar malabsorption was not demonstrated in other patients with intractable diarrhoea, severe anaemia, or pernicious anaemia during remission, but was present in two patients with hepatic cirrhosis. *P. M.-B.*

CHITRE (R. G.) & PATWARDHAN (V. N.). **Studies in Calcium and Phosphorus Metabolism. Part IV. The Absorption of Calcium from the Intestine.**—*Indian Jl. Med. Res.* 1940. Oct. Vol. 28. No. 2. pp. 361–369. [28 refs.]

In view of the widely, if not generally, accepted fact that low blood calcium in sprue is due to defective absorption, the experiments carried out by the authors on absorption of calcium from the intestine (duodenum) of normal dogs is of some interest. The salt, chloride or lactate, was introduced into the duodenum of the dogs under anaesthesia and the calcium and phosphorus in the portal blood serum and the mesenteric lymph were estimated, the calcium by Wang's method, the phosphorus by that of Bell and Doisy. It must be mentioned that they were careful to estimate the effect, if any, of anaesthesia on absorption. They found that prolonged anaesthesia (3–4 hours) was followed by a definite, though small, drop in the serum calcium.

Introduction into the duodenum was succeeded by a rise in the calcium content of the portal serum and the mesenteric lymph, showing that the portal venous system and the mesenteric lymphatics both play a part in absorption of calcium from the intestine. "No relationship was observed between the rise in Ca in the portal blood serum and (*a*) the dose or the concentration of calcium salt; (*b*) the *p*H of the solution introduced or (*c*) the pre-absorption level of Ca in blood serum." *H. H. S.*

MACKIE (Thomas T.) & MILLS (Moore A.). **Changes in the Small Intestine associated with Deficiency Disease.**—*Amer. Jl. Digestive Diseases.* 1940. Nov. Vol. 7. No. 11. pp. 480–483. [17 refs.]

The principal interest of this paper for readers of this *Bulletin* is the description of the X-ray appearances of the small intestine, indicating functional changes, which the author states are to be seen in idiopathic steatorrhoea, chronic ulcerative colitis complicated by deficiency disease, and in tropical sprue. The changes are characteristic and are most commonly seen in the duodenum and jejunum.

"The mucosal markings are coarser than normal. There is striking variation in the contour and size of the lumen and abnormal collections of gas may be present. The normal motor activity is disturbed, frequently producing a segmented distribution of the barium in dilated and isolated coils. The opaque meal usually passes through the jejunum slowly and irregularly. The filled areas show no evidence of peristalsis. At times all of the barium which has left the stomach is collected in a localized segment while the remainder of the jejunum and the duodenum

are empty. Gastric emptying is irregular corresponding apparently to the delay in the forward progress of the opaque meal through the small intestine. Although the rate of passage of the barium through the small intestine is subject to wide variation, the forward progress of the opaque meal is not more rapid than normal. A twenty-four hour residue in the cecum and ascending colon is not uncommon.

"The association of these changes with clinically obvious deficiency disease complicating ulcerative colitis, and their invariable presence in active sprue strongly suggest that they contribute to the deficiency state by interference with absorption, and thus tend to produce a vicious ascending spiral."

The actual clinical conditions investigated and reported on in this paper comprised principally ulcerative colitis; the findings in sprue are the result of previous work, see this *Bulletin*, 1936, Vol. 33, p. 64.

C. W.

MARKOFF (Nicola). Weitere Beobachtungen zur Pathogenese und Symptomatologie der einheimischen Sprue. [**Pathogenesis and Symptomatology of Non-Tropical Sprue.**]—*Schweiz. Med. Woch.* 1940. Nov. 30. Vol. 70. No. 48. pp. 1137–1139. With 2 figs. [17 refs.]

Three main lines of approach to this difficult subject can be distinguished. The disease may be due to: (1) a primary gastric lesion; (2) a vitamin deficiency; (3) a disturbance of internal secretion. The main protagonists of (1) are HANSEN and JECKLEN, of (2) CASTLE and POCK-STEEN, and of (3) VERZÀR on suprarenal and J. BAUER on pituitary. Pathologo-anatomical investigations by Jecklen have recently revealed a chronic inflammatory process in the stomach, duodenum, jejunum and ileum, and SCHEMBRA has described similar changes in the mesenteric glands. From systematic X-ray examination of the digestive tract Schembra and MOHR also distinguish chronic inflammatory changes in the duodenum and small intestine. There is apparently some connexion between this chronic intestinal disturbance and "*porphyry*." In a case under discussion the appearances were those of a paralytic ileus of the small intestine with well marked porphyrinuria which disappeared under appropriate treatment.

The symptomatic picture of sprue can be reproduced by gastro-colic fistula, changes in the pancreas, tuberculous and even lympho-granulomatous mesenteric glands. The effects of surgical resection of the small intestine can interfere with absorption of water, sugar, fats and albumin. Recently BAUMGARTNER has emphasized the importance of intestinal hurry and lack of resorption of predigested material by the large intestine consequent upon such an operation. Steatorrhoea is the principal feature and there is interference with albumin absorption although carbohydrate metabolism is maintained, and now NOETZEL has recorded the supervention of pernicious anaemia in one patient nine years after such an operation. The anamnesis of one of the cases under survey (in a man of 27) shows that the main symptoms of sprue were produced by resection for paralytic ileus of a portion of the small intestine 1·5 metres in length (iliocaecal resection with ileotransverse colostomy). The patient had undergone primary appendicectomy followed six months later by operation for paralytic ileus. The main result of the second operation was to produce steatorrhoea, grave emaciation, and macrocytic anaemia with normoblasts; osteoporotic changes also developed in the sternum, the vertebrae

and pelvis. Indican and urobilin appeared in the urine. The serum calcium was reduced to 8·4 mgm. per cent. concurrently with the appearance of Chvostek's sign. The commencement of this process lay undoubtedly in a chronic gastroenteritis. KNITTEL has also described a case in which after a perforated appendix three separate operations of small intestine resection for ileus had to be performed and in which the classical syndrome of pernicious anaemia supervened. As explaining the chronic inflammatory changes in the small intestine and their connexion with the sprue syndrome, PLUM, PREBEN & WARBURG'S observations on chronic ileitis are important. Ileitis occurs in an acute, as well as in a chronic form, and the latter may assume either the clinical picture of ulcerative colitis or of non-tropical sprue. From this observation it appears legitimate to conclude that local inflammatory changes in the ileum may lead to sprue symptoms, with a hyperchromic megalocytic anaemia responding, as does the naturally occurring disease, to liver therapy.

An illustrative case is cited of the gradual unfolding of the sprue syndrome in a man of 42 with the typical biochemical background of that disease. The main interest lay in the fact that the illness commenced as a mild gastro-enteritis, possibly and primarily due to a water-borne infection. It is concluded that everything points to a central focus of a peculiar form of gastro-enteritis and that therefore what is known as non-tropical sprue is a clinical syndrome, and not in reality a disease *sui generis*. The main location of the disease process is the whole length of the small intestine. A primary endocrine disturbance as a possible hypothesis is discarded. [The views expressed in this paper confirm those already recorded in this *Bulletin*, 1941, Vol. 38, pp. 7, 123.] *P. M.-B.*

ALLEN (J. Garrott). **The Comparative Prothrombin Responses to Vitamin K and Several of its Substitutes in a Case of Nontropical Sprue.**—*New England Jl. of Med.* 1941. Jan. 30. Vol. 224. No. 5. pp. 195–197. With 1 fig. [10 refs.]

BUTT, SNELL and OSTERBERG [*Jl. Amer. Med. Assoc.*, 1939, Vol. 113, p. 383] and ENGEL [*Med. Welt.*, 1939, Vol. 13, p. 120] have found that prothrombin deficiency may play its part in non-tropical sprue.

The reduction of plasma prothrombin in sprue probably indicates that general impairment of absorption and utilization of fats has taken place, including the fat-soluble vitamin K.

In the present communication a case of non-tropical sprue is reported in which tendency to severe haemorrhage was noted—a feature which was to some extent remedied by the administration of vitamin K. The case is of further interest in that opportunity was afforded over an eight-month period of comparing the relative antihaemorrhagic values of various preparations in the same subject. The patient had suffered for three years from signs and symptoms of sprue, including glossitis. A moderate macrocytic anaemia was present, when, after treatment on general lines for eight months, the haemorrhagic tendency declared itself by epistaxis, bleeding from the gums and ecchymosis. The prothrombin concentration was 15 per cent. of the normal, but on an " alfalfa " concentrate, in doses of 2 cc. four times daily, it reacted slowly to 38 per cent., after which no further bleeding occurred for a while, but when it fell again to 33 per cent. of the normal, haemorrhages were once more noted.

Another vitamin K substitute—2-methyl-I, 4-naphthoquinone (Lilly) in doses of 2 mgm. four times daily produced a normal prothrombin rate within 13 days. Subsequently synthetic vitamin K—2-methyl-3-phytyl-I, 4-napthoquinone (Merck) was tried out and the conclusion was reached that the second-named compound was the most active. The *raison d'être* of this study rests upon the well-established fact that the absorption of the fat-soluble vitamin K is essential for the formation of prothrombin by the liver, so that any defective absorption of the vitamin, or any impairment of production of prothrombin by the liver, may lead to prothrombin deficiency.

P. M.-B.

Childs (Alice) & Dick (George F.). **Pancreatic Function in a Case of Nontropical Sprue.**—*Arch. Intern. Med.* 1940. Oct. Vol. 66. No. 4. pp. 833–847. [43 refs.]

So far little attention has been devoted to pancreatic function or the use of pancreatic preparations in the treatment of nontropical or tropical sprue.

This subject is one of considerable difficulty since criticism has been levelled at the value of tests as indication of pancreatic function. Quantitative analyses of stool with special emphasis on the partition of fats, as well as determinations of the wet and dry weight and of total amount eliminated per day, should furnish additional information with regard to intestinal digestion and therefore with regard to pancreatic function, and these have been employed in the study under review.

A case of non-tropical sprue in a woman is here described which conformed with the points of diagnosis brought out in the literature. Chronic recurring steatorrhoea with bulky, foul-smelling stools, marked emaciation, glossitis, macrocytic anaemia, multiple vitamin and mineral deficiencies, amenorrhoea and nutritional oedema were present.

The greatest improvement in the condition of this patient occurred during the first period in hospital, where therapy consisted solely of a constant diet with a fairly high fat content and administration of pancreatic juice. The stool decreased in wet and dry weight in the percentage of fat and in the total amount eliminated daily. The fact emphasized, that pancreatic juice (Armour's pancreatin) brought about a more definite decrease than did liver extract alone, is evidence that some factor of value on intestinal digestion, possibly present in pancreatic juice, was deficient in this case. The partition of fat with low values for neutral fat and high values for soaps and free fatty acids is evidence for a definite fat splitting. It is claimed that further evidence of normal pancreatic function is furnished by the values for nitrogen in the dried stool, which never exceeded 3·5 gm. daily and by the results obtained from tests on " fasting duodenal content." The findings suggested that in a typical case of nontropical sprue there exists a deficiency in some as yet undemonstrated pancreatic factor.

With the use of dried pancreatic substance an increase of appetite occurred, but when the preparation was discontinued for an interval anorexia appeared, but appetite was regained when this preparation was resumed. The macrocytic hyperchromic anaemia present at the first admission gradually changed to normocytic hypochromic type

after pancreatic juice alone was administered. The reticulocyte response was greatest after oral administration of liver extract at a time when the haemoglobin concentration and the erythrocyte counts were at their lowest. *P. M.-B.*

O'Sullivan (John F.). **Gee-Thaysen Disease : (Idiopathic Steatorrhoea of Adults and Adolescents in Non-Tropical Countries).** With a Note and a Postscriptum by Henry Moore.—*Brit. Med. Jl.* 1941. Feb. 8. pp. 183–187. [14 refs.]

This paper may be considered as a further contribution to the vexed subject of the steatorrhoeas and as an attempt to stabilize the somewhat bewildering nomenclature which has cluttered up this subject. As coeliac disease was first described by Samuel Gee in 1888, and the condition as it occurs in adults was extensively studied by Thaysen (1929–1932), the cognomen of Gee-Thaysen disease is retained as first suggested by Moore, O'Farrell, Geraghty, Hayden & Moriarty in 1936 and later supported by Mogensen (1937), whilst Gee-Herter disease is suggested for the infantile form.

The paper concerns itself with two cases, taking into consideration the recent work of Kantor (1939) upon a further diagnostic feature in the radiographic appearances of the small intestine, such as the obliteration of the usual markings of the valvulae conniventes ("moulage sign") and dilation with segmentation of the contained barium into "clumps." In neither of the two cases could it be said that Kantor's findings were evident. In the treatment of the two cases the authors were guided by the experiments of Barker & Rhoads who found in tropical sprue that parenteral administration of liver extracts exerts a specific effect upon the absorption power of the small intestine, and the experience of Snell (1939) who showed that the radiographic appearances of the small intestine were restored to normal by the same therapy.

The first case was that of a single man of 28 with steatorrhoea, whose stools upon regulated hospital diet weighed 40 oz. daily and in whom other features tallied with the generally accepted description of the disease. Beard and moustache were absent ; the testicles were small and there were other signs of infantilism. Radiographic examination showed that the epiphyses of the lower ends of the ulnae were united to the shafts, whilst those of the lower ends of the radii, tibiae and femora were but partially united. The bones of the hand showed a moderate degree of bony sub-calcification. There was marked redundancy and dilation of the colon. The patient was put on a low-fat diet consisting of 218 gm. carbohydrate, 88 gm. protein and 77 gm. fat. Therapy consisted of 25 minims of dilute HCl. with pepsin, thrice daily after meals, 9 grains of ferrous sulphate, 40 gm. calcium gluconate, 25 mgm. calciferol and a vitamin preparation furnishing a daily intake of 18,600 I.U. vitamin A, 150 I.U. vitamin B., 30 Sherman units B_2, 600 I.U. vitamin C and 2,700 I.U. of vitamin D. Under this treatment the bulk of faeces was reduced to 22 oz. daily—diarrhoea relieved and steatorrhoea reduced from 75·47 to 34·48 gm. total lipoid in 24 hours ; there was a gain in weight of more than 42 lb. and an increase of an inch in height. The diagnosis of Gee-Thaysen disease might be called in doubt because of the high faecal nitrogen (8·34 gm.) which would suggest pancreatogenous diarrhoea, but other

features—the flat sugar-curve and the absence of muscle fibres in the stools, as well as the general clinical course of the case—negatived this suggestion.

The second case was in a man of 19 years with pronounced anaemia and brownish pigmentation over the malar regions, beard and moustache being absent. Examination showed a slight degree of hypocalcaemia, steatorrhoea, infantilism, non-union of epiphyses and a severe degree of anaemia. Treatment was conducted on lines similar to the first, reinforced with four courses of intramuscular liver extract, 2 cc. daily for four days. A most satisfactory clinical response was produced, the anaemia rapidly disappeared and the improvement was accompanied by the disappearance of the heart murmurs and a striking change in the patient's appearance. For the past year the only treatment has been a low fat diet, 25 minims of dilute HCl. with pepsin thrice daily after meals. After a year's interval he had gained 33 lb. in weight and 2 ins. in height and is now an active healthy medical student.

In this second case the high percentage of neutral fat (21·68 per cent.) is discussed. FOWWEATHER (1926) has stated that, where neutral fat exceeds 11 per cent. of the dry matter, defective fat splitting should be suspected, but if total split lipoid exceeds 16 per cent. of the dry matter, deficient fat absorption is present. The probable explanation is the rapid rate at which the food passes through the intestine and the consequent failure of the pancreatic ferments to exert full action. In this instance, after treatment, the percentage of neutral fats fell to 6·25 per cent.—which is well within normal limits. To both these patients an allowance of 2 gm. protein per kilo. body weight was made—an equivalent of 90 gm. daily—which is considered advisable.

Prof. MOORE contributes some individual observations to the effect that in the great majority of cases the fundamental fault lies in imperfect absorption from the small intestine, though in a small minority lacteal obstruction may possibly play a part. The most important factor seems to be imperfect lipoid absorption, so that the abnormal amount of these bodies in the bowel is responsible for the diarrhoea, and also for imperfect calcium, phosphorus, haematopoietic bodies and vitamin absorption. He has followed up 11 out of the 12 cases previously reported upon for a period of 14 months to 15 years, seven for over five and two for over three years. After the initial period of low-fat diet and "replacement" therapy, seven remained in good health for prolonged periods on low-fat diet alone. His experience, contrary to the view usually held, is that results of treatment are most satisfactory, notwithstanding that six out of the 12 could be classified as very severe and four as less so; three had multiple pathological fractures which yielded to treatment, and yet only one died of the disease itself, others of pneumonia and tuberculosis, whilst of the nine surviving up to date, six are in excellent health. Arising out of the paper of BENNETT and HARDWICK, Moore believes that the one aetiological factor running through coeliac disease, in infancy or persisting to adult life, in idiopathic steatorrhoea beginning adult life, or tropical sprue, is "chronic jejuno-ileal insufficiency," but the *manifestations* of this deficiency probably differ according to age, the time of onset, duration, environment and other factors. With such a common fundamental defect it may not be easy to say whether an adult case is more closely allied to tropical sprue than to infantile coeliac disease. [See also this *Bulletin*, 1941, Vol. 38, p. 274.] *P. M-B.*

PELLAGRA AND OTHER DEFICIENCY DISEASES.

Précis of Abstracts in this Section.

Sutton and Ashworth (p. 397) report cases of pellagra in which the symptoms responded to extract of the pituitary gland, but which relapsed when this treatment was discontinued. Beguiristain (p. 397) describes a case of atypical pellagra in which he suspected disturbance of the suprarenals.

Simpson (p. 398) describes a fatal case, in which a diagnosis of pellagra was made, in a girl in England. Jersild (p. 398) describes a case of pellagra in which psychic symptoms were not relieved by nicotinic acid but responded to liver extract.

Elvehjem (p. 398) discusses methods of assaying nicotinic acid and the content of this substance in articles of diet. The deficiencies of other members of the vitamin B complex in pellagra are discussed. It is concluded that only nicotinic acid and related substances have potency against black tongue of dogs. The coenzyme 1 content of animal tissues is discussed, and the nicotinic acid content of tissues of animals suffering from deficiency in that substance.

Najjar and Holt (p. 400) discuss a blue fluorescent substance in urine which is apparently a measure of the store of nicotinic acid in the body and which is absent in pellagra. They describe a second fluorescent substance, not normally present, which is found in the urine in pellagra, and discuss the significance of these findings. Baserga and Fornaroli (p. 400) describe a method of estimating nicotinic acid in urine and the response to the administration of 150 mgm. A low reading is regarded as an indication of deficiency.

Jiménez García (p. 401) describe cases of glossitis observed in Madrid during the Spanish Civil War when the diet of the population was seriously inadequate, especially in vitamin B_2. Some of the patients recovered in spite of the deficiencies in the diet, but in others retrobulbar neuritis, neuritis of the auditory nerve and pellagra developed. There were disturbances of sensation and neuralgias; hypochlorhydria was common and indicanuria occurred. The value of treatment was difficult to assess, since the tendency was towards recovery, but the results with nicotinic acid were variable. Brewers' yeast was apparently beneficial.

van Veen and Dhanoedibroto (p. 402) record cases of nutritional oedema in Central Java. The syndrome is not distinct and clear cut, and is complicated by malaria, dysentery and hookworm disease. Low blood nicotinic acid values were found, but it was observed that these were not directly connected with pellagra-like symptoms exhibited by some of the patients, but were closely connected with low blood cell volumes.

Spies *et al.* (p. 404) have endeavoured to find some easily stored and palatable food having the same therapeutic properties as yeast and liver extracts, since they found that patients did not take the latter for long periods when released from supervision. Peanut butter blended with brewers' yeast powder was found to be suitable; it tends to prevent pellagra, beriberi and riboflavin deficiency.

Efremov (p. 405) describes lesions, which resembled each other, in animals given diets deficient in vitamin B_6, riboflavin and nicotinic

acid. The skin lesions of human pellagra most closely resemble those of vitamin B_6 deficiency in rats, but the complete picture of human pellagra cannot be produced in animals.

Bichel and Meulengracht (p. 406) report pellagrous skin changes originating in a patient who had been under treatment with riboflavin. Hou (p. 406) describes a syndrome, apparently due to ariboflavinosis, in Chinese in Shanghai. The lesions are chiefly ocular and, unlike cases described in America, there are few affections of the lip and tongue. Riboflavin produces rapid cure, but vitamin A and nicotinic acid have no effect.

Clark (p. 406) points out that cheilosis is common in West Africa in people whose diet consists largely of cassava, which is rich in riboflavin, and explains this anomaly on the hypothesis that this food contains a cyanogenetic glucoside, linamarin, the consumption of which inhibits the action of the suprarenals which normally phosphorylate riboflavin. He postulates a similar substance in maize, and concludes that five times as much riboflavin is needed to preserve health in subjects fed upon maize diets as in those on monotonous diets without maize. Davis comments on these views. *C. W.*

Sutton (Don C.) & Ashworth (John). **Interrelation between the Vitamin B Complex and the Anterior Lobe of the Pituitary Gland.** —*Jl. Lab. & Clin. Med.* 1940. Aug. Vol. 25. No. 11. pp. 1188–1192. With 2 coloured plates.

To state the authors' conclusions first: "Evidence is presented indicating that an extract of the anterior lobe of the pituitary gland will cause recovery of pellagra lesions when they have failed to respond to nicotinic acid and riboflavin, parenteral liver and adequate diet."

Two patients came under observation suffering from diarrhoea, loss of weight, oedema of the feet, glossitis, gastritis, achlorhydria, proctitis and minor mental changes, but no dermatitis. As no response to nicotinic acid was obtained, the diagnosis of pituitary cachexia was considered and an extract of pituitary gland was given with excellent results. Three cases of pellagra with typical dermatitis on face, hands and feet, and affection of the scrotum and angles of the mouth, glossitis and diarrhoea were then given the same treatment. All three showed rapid response but relapsed a few days after the treatment was discontinued. The preparation used was polyansyn (Armour & Co.) and 2 cc. intramuscular injections were given daily.

H. S. Stannus.

Beguiristain (J.). Un caso de sindrome incompleto y anómalo de pelagra. [**A Case of Pellagra with Anomalous Symptoms.**]—*Rev. Clín. Española.* Madrid. 1940. July 1. Vol. 1. No. 1. p. 55.

The patient was a man of 50 years, whose diet for the last 18 months had comprised exclusively bread, potatoes and a little fat. In September 1939 he had lost 20 kgm. in weight, showed generalized hyperpigmentation, ichthyosis, and weakness so that he could scarcely stand. The pigmentation was most marked on the legs, genitalia and trunk (the patient was verminous), less on face, arms and hands. There were crusts of impetigo and pyodermatitis on legs, forearms,

neck, hands and face. Blood examination gave red cells 2,800,000, white 10,640 per cmm. ; polymorphonuclears 77 per cent., lymphocytes 15, monocytes and eosinophils each 4 per cent. Facies and gait were Parkinsonian.

The diet was rectified and in a month the patient gained 4 kgm. in weight. By the following February he had gained another 3 kgm. and the pigmentation was much less noticeable. The pyodermal crusts separated, leaving unpigmented atrophic skin, imparting a mottled appearance to the thighs, legs and forearms. He was now given fresh brewers' yeast and improved rapidly. By March he was able to take exercise in the open and in 18 days gained more than 5 kgm. Blood examination gave : red cells 4,500,000 per cmm., white 9,000, relative percentages about the same as before. There remained the Parkinsonism with rigidity and tremor of legs.

There was notable absence of the mouth and tongue lesions of pellagra and the author suggests that there may have been adrenal disturbance to account for the pigmentation and debility. *H. H. S.*

SIMPSON (R. E. Hope). **Fatal Pellagra in an English Schoolgirl.**—*Lancet.* 1940. Nov. 9. pp. 589–590.

In May, with the first constant sunshine, the patient, a girl of 13, developed a rash on arms, legs, face and neck. This resembled exaggerated sunburn and there was some dry exfoliation. In August there was stomatitis and gingivitis and some fever ; these improved in a few days with treatment for Vincent's angina, but the rash remained. The blood picture was normal except for slight polymorphonuclear leucocytosis. When the patient was apparently recovering she had a convulsion, the rash became dusky blue-purple and innumerable tiny vesicles appeared on the knees, elbows and neck ; she was cyanosed and confused and died in a few hours after passing into status epilepticus.

The patient was tall and thin, had always refused milk and had always eaten much bread and butter ; vegetables had been available to her but meat had probably been restricted. There are four healthy siblings. The author regards the condition as pellagra. *C. W.*

JERSILD (Mogens). 2 Tilfaelde af Pellagra. [**Two Cases of Pellagra.**] —*Nordisk Med.* 1941. Feb. 8. Vol. 9. No. 6. pp. 426–428. With 2 figs. English summary.

" In one patient recovery was obtained at once after treatment with nicotinic acid. In the other case—although the skin symptoms vanished—haemorrhagic diarrhoea and psychical changes were noticed during treatment with nicotinic acid. These symptoms vanished after injection of Becoplex (Ido-preparation produced from fresh liver containing all components of the B-vitamin complex)."

ELVEHJEM (C. A.). **The Biological Significance of Nicotinic Acid.**—*Bull. New York Acad. Med.* 1940. Mar. Vol. 16. No. 3. pp. 173–189. With 1 fig. [56 refs.]

The substance of this communication, the Harvey Lecture delivered in November 1939, comprises a valuable review of the biochemistry of nicotinic acid, together with some recent results of investigations undertaken in the author's laboratory.

Methods of determining the nicotinic acid content in various foodstuffs and tissues include chemical procedures, bacterial growth methods and animal assays. The author considers the most satisfactory chemical method to be that in which the pyridine nucleus is broken down by cyanogen bromide and aniline to give a yellow compound which is measured colorimetrically. For animal assays, dogs are employed. Black tongue is produced in them by a basal diet, details of which are given in the text, and subsequently the therapeutic response of each animal to various measured quantities of diet is compared with that previously evoked by standard amounts of nicotinic acid. The results of such bio-assays of a number of different articles of diet are summarized in a table in the text. Liver was found to contain 1·2 mgm. per gm. dry weight. Assuming a daily human requirement of 25 mgm. nicotinic acid, it is concluded that $\frac{1}{4}$ lb. of fresh liver or $\frac{1}{2}$ lb. lean meat will suffice. In general, natural foods contain from 1 to 100 mgm. of nicotinic acid per 100 gm. dry material.

Attention is drawn to the probable deficiency in pellagra of other members of the vitamin B complex. In this connexion it is of interest to note that dogs deprived of vitamin B_6 develop a severe microcytic anaemia which readily responds to synthetic vitamin B_6; while if the diet is supplemented with vitamin B_6 alone, growth is arrested until pantothenic acid and factor W are added.

As a result of an examination for anti-black-tongue potency of a number of related compounds, the author concludes that this property is possessed only by nicotinic acid, its amide and those compounds, listed in the text, which are capable of oxidation or hydrolytic conversion to these substances in the animal body.

The relationship between nicotinic acid and coenzyme 1 has been studied in the author's laboratory by the yeast fermentation method which is based on the principle that the addition of varying amounts of coenzyme 1 to a washed yeast preparation will produce rates of fermentation proportional to the amount of coenzyme 1 added. The results are given of estimations of the coenzyme 1 content of the tissues of several animal species. In spite of apparent differences in nutritional requirements there is relatively little variation in the figures for the different species.

Estimations on dogs and pigs suffering from severe nicotinic acid deficiency were compared with those of normal animals. In blood, brain and kidney no appreciable difference was detected in the coenzyme 1 content of the two groups, but in liver and muscle from deficient animals there was a significant decrease as compared with the same tissues from normal animals.

The author's studies on human beings confirm the findings of Kohn in that nicotinic acid deficiency does not result in a blood coenzyme 1 level below that found in normal subjects, *i.e.*, 20–30 micrograms per cc. Excessive ingestion of nicotinic acid may, however, temporarily double the concentration of coenzyme 1 in the blood.

In conclusion the author affirms the probability that the rapid response of deficient human beings and animals following administration of nicotinic acid may be due to formation of coenzyme 1 when the nicotinic acid part of the molecule is made available. The rôle of coenzyme 2 in the metabolism of nicotinic acid is briefly discussed, but acquisition of accurate data awaits improvement in technical methods.

L. J. Davis.

NAJJAR (Victor A.) & HOLT (L. Emmett), Jr. **The Excretion of Specific Fluorescent Substances in the Urine in Pellagra.**—*Science.* 1941. Jan. 3. Vol. 93. No. 2401. pp. 20–21.

In a previous communication Najjar and WOOD [this *Bulletin*, 1940, Vol. 37, p. 798] showed that the amount of a blue fluorescent substance in the urine was apparently a measure of the store of nicotinic acid in the body. It has now been demonstrated that this substance is absent from the urine of pellagrins and that the ingestion of nicotinic acid, and other pyridine derivatives having anti-pellagra activity, causes the reappearance of this substance. They have further shown that in the urine of pellagrins there appears a second substance not normally present which gives a whitish blue fluorescence without an alkali addition to the eluate after adsorption on zeolite and treatment with KCl. This they refer to as F_1; the substance previously demonstrated as F_2. Neither has been identified.

In pellagra the disappearance of F_2 appears to take place first, as the disease progresses F_1 increases in amount. Treatment with nicotinic acid reverses the process. The authors suggest that normally an enzyme of which nicotinic acid is a component converts F_1 to F_2. In nicotinic acid deficiency states this fails to occur and F_1 accumulates. In black tongue of dogs similar phenomena have been found.

H. S. S.

BASERGA (A.) & FORNAROLI (P.). Schnelle Orientierungsmethode zur Aufdeckung des Mangels des PP-Faktors. [**Rapid Method for the Discovery of Deficiency in the PP Factor.**]—*Klin. Woch.* 1940. Sept. 21. Vol. 19. No. 38. pp. 988-989. With 3 figs. [11 refs.]

The necessary reagents are :—

1. Buffer solution, KH_2PO_4, 7·04 gm., Na_2HPO_4 [quantity not stated in the paper] in 100 cc. water.
2. Freshly prepared brom-cyanide solution, made by adding 50 per cent. KCN solution to saturated bromine water until the colour just disappears.
3. Saturated solution of aniline.

Eight cc. of fresh clear urine are mixed with 2 cc. of solution 1, 5 drops of solution 2 and 5 drops of solution 3. After exactly 6 minutes the mixture is examined in a Zeiss graduated photometer with a 10 mm. cell and S45 or S47 filter. A control is employed by substituting 5 drops of water for the 5 drops of solution 2.

The procedure is to estimate by this test the nicotinic acid content of the first morning urine of the patient who, after passing it, is given 150 mgm. nicotinic acid in three parts within half hour. The nicotinic acid content is again estimated in the total urine passed within the next six hours; the difference between the readings is related to the amount of urine passed and the total excreted is calculated. During this period no coramine or sulphapyridine must be taken and the patient must not smoke.

Low readings (of less than 1 mgm.) have been found in Lombardy in people who, though showing no overt signs of pellagra, are living on a low protein diet. A low reading is therefore an indication of deficiency.

C. W.

KOCHHAR (B. D.). **The Quantitative Estimation of Nicotinic Acid in Blood and Other Body Fluids.**—*Indian Jl. Med. Res.* 1940. Oct. Vol. 28. No. 2. pp. 385–396. [13 refs.]

HARRIS (Seale). **The Genesis of Pellagra.**—*Southern Med. Jl.* 1940. Oct. Vol. 33. No. 10. pp. 1044–1053. With 1 fig. [45 refs.]

ORMSBY (Oliver S.). **Pellagra.**—*Proc. Inst. Med. Chicago.* 1940. Dec. 15. Vol. 13. No. 9. pp. 230–243. [35 refs.]

JIMÉNEZ GARCÍA (Francisco). Estudio clínico de los trastornos carenciales observados en la población civil de Madrid durante la guerra (1936–1939). I. Glositis simple. [**Clinical Study of Avitaminosis among the Civil Population of Madrid during the Civil War (1936–39). I. Simple Glossitis.**]—*Rev. Clin. Espanola.* Madrid. 1940. Sept. 1. Vol. 1. No. 3. pp. 231–238. With 6 figs. [21 refs.] French summary p. 237.

Early in 1937 sporadic cases of glossitis were coming under the author's observation and he noted as time went on that, in spite of the patients remaining on the same poor diet as before, some recovered, others passed into a chronic stage which, though at first regarded as a pre-pellagrous condition, did not develop into pellagra.

The author has carefully followed up 336 patients whom he classed as typical of "simple glossitis." During the 32 months of the war there must have been several thousand cases. The majority of the 336 personally observed by the author were between 20 and 35 years of age, but the limits were one month and "old age"; about three times as many women as men were attacked. Loss of weight was marked, the average being a little over 20 per cent., but some lost much more. Most cases were seen in the last four months of 1938, during which an epidemic outbreak of simple glossitis occurred among the troops encircling Madrid. Some of the patients showed more serious "deficiency" symptoms and retrobulbar optic neuritis as described by Fitzgerald MOORE in Nigeria [see this *Bulletin*, 1936, Vol. 33, p. 889], neuritis of the VIIIth cranial nerve and pellagra.

The nutrition of the civil population during the war was certainly inadequate; its caloric value was under 1,000; proteins were less than half the "necessary minimum" for health and most of them were of vegetal origin; minerals and vitamins were much reduced, especially the vitamin B_2 complex. The daily diet for an adult contained protein 41·3 gm., fats 12·9 gm., carbohydrates 169·6 gm., calorie value 957. It is difficult to determine accurately how long would elapse on this diet before the glossitis appeared, but it seemed to be 4–5 months.

Clinically the cases could be fairly readily grouped as acute, subacute and chronic, the percentage proportions being approximately 8, 82 and 10 respectively. The different forms, or, rather, stages are described in detail in the article, but this need not be repeated here.

Later symptoms were varied and included visual disturbances such as dimness of vision, scotomata, diplopia, and even actual retrobulbar optic neuritis; acroparaesthesias; formication, numbness, pricking sensations; neuralgia and pain in palms and soles; vomiting occasionally, diarrhoea more commonly. Of 80 patients specially examined, 41 had achlorhydria, 32 hypochlorhydria and only 7 were normal in this

respect. Most of those with subacute benign glossitis had hypochlorhydria or normal acidity, those with achlorhydria were the acute, the more serious subacute and the chronic cases. Indicanuria was common.

As regards the course of the disease; those with the acute form after a period of days or weeks in a subacute stage, might rapidly clear up; the subacute might recover completely in 1–2 months, the chronic might continue for 5–6 months or even a year. Unless the more serious complications mentioned above supervened the trend was towards cure spontaneously, hence the difficulty of assessing the value of any treatment adopted. Diagnosis had to be made from pellagrous glossitis, pernicious anaemia and sprue. Various lines of treatment were followed: lemon juice, vegetarian diet, chlorate of potassium, nitrate of silver, mercurochrome, iodized glycerin, cod liver oil, vitamin A, C, B_1, B_2, lactoflavin, nicotinic acid, liver preparations, and so on. Vitamin B in the form of brewers' yeast did good; the results with nicotinic acid varied. Those with acute glossitis and those with intestinal disturbance did best, and in the latter the intestinal and tongue symptoms improved together. It is only right to say, however, that many patients showed no amelioration when treated with nicotinic acid.

The author sums up his conclusions thus:—

1. The glossitis seen in Madrid, either as a single symptom or associated with other slight "deficiency" signs is a separate condition [he uses the term "distinct entity"] called by him simple glossitis.

2. Aetiologically, it is a nutritional deficiency of vitamin B_2 complex—deficiency of some factor at present unknown, and not of nicotinic acid or riboflavin.

3. The reduction or absence of this factor which causes simple glossitis is common to all the processes of which glossitis is a symptom—pellagra, paraesthesias, retrobulbar neuritis, ulcerative colitis, pernicious anaemia, sprue.

4. The reduction of this factor was manifested early and in a constant manner in Madrid.

5. This form of glossitis is not benefited therapeutically by vitamins A, B_1, C, D, or riboflavin, and the effect of nicotinic acid is variable.

6. The most efficacious form of treatment is by brewers' yeast or its extracts containing the vitamin B_2 complex. *H. H. S.*

VAN VEEN (A. G.) & RADEN SARDJONO DHANOEDIBROTO. Over nicotinezuurbepalingen bij voedingsoedeempatiënten in Midden-Java. [**Nicotinic Acid Determination in Nutritional Oedema in Central Java.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1940. July 2. Vol. 80. No. 27. pp. 1622–1637. With 1 chart. [Refs. in footnotes.] English summary.

"In the region around about Pemalang (Central Java) nutritional oedema occurred rather frequently in the year 1939. Its fundamental cause is to be found in a number of successive failures of crops. It is a remarkable fact, however, that, although the nutrition in these parts was deficient in many respects, only oedema and sometimes slight 'pellagra-like' symptoms but no other deficiency symptoms have been observed.

" Diet surveys were held at Pemalang by the Institute for Nutrition Research and also medical examinations were made. At the Eykman Institute a number of analyses were done regarding vitamin A, B_1, nicotinic acid and proteins in the blood of oedema cases and their families.

" In the publication in hand special attention is paid to the concentration of nicotinic acid in the blood of nutritional oedema cases (immediately after their entering the auxiliary hospital at Moga) of whom a certain number showed pellagra-like symptoms. Through lack of time and staff it was impossible to examine the patients thoroughly and to keep them under accurate observation, nor could any therapeutic experiments be made on a large scale.

" In consequence of the fact that the nutrition had been deficient for a long time and in practically every respect, it was to be foreseen that no pure and uniform deficiency-syndromes would appear. Moreover these syndromes were blurred by ankylostomiasis, which is a frequent concomitant of poor nutrition, and sometimes by various other diseases (malaria, dysenteries).

" In some cases low nicotinic acid contents were found in the urine ($\pm$ 50 γ/100 cc.). Since, with the handicaps attending the investigation it was impossible to get the 24 hours' volumes of urine or to learn whether any anureses or strong diureses were present when the patients entered hospital, these determinations do not have great value. For that reason they are not discussed in this publication. More attention was paid to the determination of the nicotinic acid level in the blood, after a technique combined from SWAMINATHAN'S and BANDIER'S. Low nicotinic acid levels did frequently occur in the blood of the oedema cases in the hospital. They were however not to be directly connected with the slight pellagra-like symptoms described in this publication, nor with the so-called ' porphyrin ' reaction of BECK-ELLINGER-SPIES, which is no real porphyrin test. On the other hand we found a rather close connection with the blood-cell volume (as determined by the haematocrit) in the sense that a low nicotinic acid level is in our patients almost always attended by a low cell-volume, which was of frequent occurrence in these chronically underfed, mostly very anaemic oedema cases. This connection between nicotinic acid content and haematocrit value depends on the fact that nicotinic acid does not occur in the blood serum.

" With a normal cell volume a normal nicotinic acid level was usually found, but at the same time pellagra-like dermal symptoms would sometimes occur.

" The state of affairs with our nutritional oedema cases is therefore like this : most likely not only the food (principally Indian corn) is deficient in nicotinic acid, but also the conveying intensity of the blood for nicotinic acid is often reduced by the low cell volume.

" It would be interesting to know whether low cell volumes also play an important part with regard to the nicotinic acid supply of people with a classical pellagra. We have not been able to find any data on this subject in the literature except one single publication by MACHWILADSE, in which we find mentioned that the number of erythrocytes and also of leucocytes is mostly reduced in pellagra cases, without however having any direct connection with the seriousness of the case. If these observations generally held good one might always expect low nicotinic acid levels in the blood of pellagra cases. In this connection it may be interesting to note that LWOFF and his

co-operators found normal nicotinic acid levels in 10 pellagra cases, although they followed another technique than we did. It is a pity that no haematocrit values are mentioned by them.

" Finally we have to mention certain observations made by KÜHNAU who found in the blood of some pellagra cases nicotinic acid values varying between 70 and 180 mg. per cent., *i.e.* of the same magnitude as we found in many nutritional oedema cases. The nicotinic acid secretion in the urine of his patients was lowered, to be sure, but not at all very low, although the pellagra symptoms were very characteristic : erythemata, here and there scaly skin with bladders on the back of the hand, brown pigmentations, follicular hyperkeratoses in the face, areflexia and diarrhoea. So he comes to the conclusion, that although therapeutically the effect of nicotinic acid in pellagra may be very striking, yet the connexion between this disease and the nicotinic acid level is not quite so simple.

" The brief result of our investigation is that the nicotinic acid level of the blood of many nutritional oedema cases proves to be very low. The low nicotinic acid content (which on the one hand may be expected in consequence of the probably nicotinic acid-deficient nutrition of the population) was not connected with the sometimes occurring pellagra-like symptoms, but with the low cell volume (haematocrit). Because of the importance of nicotinic acid for the organism (not only as connected with pellagra but also with regard to blood formation) the occurrence of these low nicotinic acid levels is an unfavourable symptom."

SPIES (Tom D.), GRANT (H. M.) & GRANT (J. M.). **Observations on the Effectiveness of a Yeast-Peanut Butter Mixture in Vitamin B Complex Deficiencies. A Progress Report.**—*Southern Med. Jl.* 1941. Feb. Vol. 34. No. 2. pp. 159–161. [Summary appears also in *Bulletin of Hygiene.*]

The value of yeast and liver extracts in the relief of symptoms due to deficiency of the vitamin B complex has been generally recognized, but whilst patients take these substances when under supervision, they refuse to continue to do so for long periods at home. It thus became desirable to substitute some more easily stored and palatable food having the same therapeutic properties. The most important of these is the peanut ; it is efficacious in the gradual relief of mild deficiencies due to lack of water-soluble vitamins, and in supplying a considerable quantity of energy material and protein of good quality, but the results per unit of weight have not been so good as those with high-grade brewers' yeast. It was then considered desirable to fortify peanut butter with synthetic vitamins or with yeast or liver extract. This mixture proved to be acceptable and pleasing up to a composition of 25 per cent. yeast.

The Anheuser-Busch, Inc., organization has supplied a commercial peanut butter blended with strain K-A residual brewers' yeast powder. Twenty-five malnourished patients with mild pellagra, beriberi or riboflavin deficiencies were selected and studied. At the time of admission they were underweight and presented lesions diagnostic of one or more deficiency diseases. Each patient was given peanut butter containing 15 per cent. brewers' yeast *ad lib*, twice daily, and by the end of a week it became evident that the patients would continue to eat the mixture even when the yeast content was increased to 25 per cent.

It was then found desirable to replace 8 per cent. peanut butter with peanut oil. Some patients complained of a bitter taste of the " strain K " mixture, but no complaints were made when " C-50 " yeast was used. The majority of patients observed for two months consumed on an average 60–75 gm. of the mixture daily and a few as much as 160 gm. In most instances the appetite improved and the patients gained in weight.

It would be misleading to compare the gradual improvement in this series with the spectacular clinical remissions and even life-saving effects caused by large doses of nicotinic acid in pellagra, or by riboflavin in ariboflavinosis, or by thiamin in vitamin B_1 deficiencies. It is estimated that 50 per cent. of the American people fail in optimum health and vigour because of low vitamin B intake. The authors therefore find that a mixture containing 25 per cent. brewers' yeast powder, 67 per cent. peanut butter and 8 per cent. peanut oil is an inexpensive, palatable food mixture which tends to prevent pellagra, beriberi and riboflavin deficiency. Two ounces or more of this *per diem* used as a supplement to the diet gradually improves the health of persons with subclinical symptoms of deficiency disease.

P. Manson-Bahr.

Efremov (V. V.). **Experimental Avitaminoses of the B2-Complex Group and Pellagra of Man.**—*Acta Med. URSS.* 1939. Vol. 2. No. 4. pp. 622–630.

Lesions of a rather similar type were produced in rats, dogs and monkeys by diets deficient in vitamin B_6, riboflavin or nicotinic acid. The most frequent lesions noted were : (1) erythroedema (B_6 deficiency in rats) or alopecia (riboflavin deficiency in rats and nicotinic acid deficiency in dogs and monkeys). None of these skin lesions was accentuated by sunlight ; (2) stomatitis and glossitis (B_6 deficiency in rats), and various gastro-intestinal symptoms, which were not associated with any obvious tissue changes, in all species ; (3) nervous disorders such as loss of muscle tone, ataxia, incoordination and paraplegia. Degenerative changes were found in varying degrees in the medulla, the postero-lateral columns of the spinal cord, and the posterior roots. There were also localized degenerations of various nerves in rats and degenerative changes in the ganglion cells of the cortex, cerebellum and stem nuclei in dogs and monkeys. A study of the skin lesions of human pellagra showed that they most closely resembled those of B_6 deficiency in rats. Exposure of pellagra patients to sunlight did not produce erythema and it appeared to be brought about by various types of irritation. All the patients showed disturbances of gastric secretion, and, unlike what may be seen in animals, atrophic gastritis leading to a form of ulcerative colitis occurred. Sore mouth and glossitis were often seen and in grave cases secondary infection occurred. Dogs and monkeys, however, showed no changes in the mouth or tongue and the condition of " Black Tongue " of dogs was not produced by a diet deficient in nicotinic acid. The greatest resemblance between human pellagra and animals deficient in components of the B_2 complex, was in the nervous lesions. All showed a picture resembling subacute combined degeneration whilst in man and dogs and monkeys degenerative changes in the ganglion cells of the brain were prominent. It is

concluded that owing to the varying susceptibility of tissues in different animals the complete picture of pellagra in man cannot be produced in animals. Deficiencies in any part of the B_2 complex may give rise to some lesions resembling those of human pellagra.

H. N. H. Green.

BICHEL (Jørgen) & MEULENGRACHT (E.). Pellagra opstaaet efter Behandling af Plummer-Vinson Syndrom med Riboflavin. [**Onset of Pellagra after Treatment of the Plummer-Vinson Syndrome with Riboflavin.**]—*Nordisk Med.* 1941. Jan. 18. Vol. 9. No. 3. pp. 185–187. With 1 fig. English summary (5 lines).

"The authors report the case of a patient in whom treatment with riboflavine for a considerable period was followed by the appearance of pellagrous changes in the skin. They discuss the possibility of a connexion between the riboflavine taken in and the development of these cutaneous changes."

HOU (H. C.). **Riboflavin Deficiency among Chinese. I. Ocular Manifestations.**—*Chinese Med. Jl.* 1940. Dec. Vol. 58. No. 6. pp. 616–628. With 5 figs. on 2 plates. [19 refs.]

The author has discovered that a certain group of ocular manifestations is not uncommon among the Chinese of Shanghai. The lesions, it is believed, are due to an ariboflavinosis, inasmuch as they clear up with the administration of riboflavin. Patients exhibiting these signs form about 9 per cent. of those attending an eye clinic. Forty cases were studied, including four which also had the symptoms of frank pellagra. The lesions observed, in order of frequency, were: pericorneal injection, bulbar conjunctivitis, photophobia, vascularization of the cornea, blurring of vision, phlyctenules, corneal opacities, corneal ulcers, blepharitis and iritis. They thus resemble those cases described by American writers. There are, however, two points of difference. Phlyctenules have not before been noted in this syndrome and while American observers find a pretty close association of these ocular manifestations with "cheilosis," glossitis and seborrhoeic dermatitis, among the Chinese affections of lip and tongue occurred in comparatively few.

The condition cleared up in from 2–7 days on treatment with riboflavin by mouth—5 mgm. thrice daily for 2 days, twice daily for 3 to 10 days and then once daily for a further 7 days. Vitamin A and nicotinic acid had no effect.

The author suggests that lack of riboflavin may be a factor in all cases of phlyctenular disease. *H. S. S.*

CLARK (Alfred). **Concerning Riboflavin.**—*Jl. Trop. Med. & Hyg.* 1941. Feb. 1. Vol. 44. No. 3. pp. 15–17.

Dr. Clark has previously suggested that pellagra may be the result of disordered metabolism due to the ingestion of cyanides in the food. In the present communication he enlists further support for his hypothesis from the consideration of the circumstances determining the

prevalence of cheilosis in various communities. Cheilosis is the syndrome of skin lesions around the mouth, frequently associated with pellagra, which has been attributed by SEBRELL to riboflavin deficiency.

The author points out that this condition is common in West Africa among those classes whose diet consists largely of cassava, which is rich in riboflavin. This anomaly he explains by the presence in cassava of a cyanogenetic glucoside, linamarin. Reference is made to the work of VERZER *et al.*, claiming phosphorylation of riboflavin to be a normal function of the adrenals which is inhibited by the presence of cyanides, and attention is drawn to the significance in West Africa of "the great frequency of the occurrence of cheilosis and of adrenal lesions." [No reference is quoted in support of this statement].

The thesis is then developed that a substance of similar inhibitory activity may be present in maize; mandelic nitrile is suggested. Lists of diets with the riboflavin contents of the various articles of food are submitted, and it is pointed out that cheilosis is not observed among English working classes on diets comparing unfavourably in riboflavin content with the maize-containing diets given to inmates of the Kumasi Gaol Infirmary. The data of Sebrell, working in Georgia, U.S.A., are also quoted, and it is concluded that "five times as much riboflavin is needed to preserve health in subjects fed upon the maize-containing diet as is required for people on a very monotonous diet without maize."

[The evidence upon which the author's conclusions are based does not appear to be unassailable. Further work is desirable before cheilosis, or angular stomatitis, deserves critical acceptance as a pathological entity due essentially to riboflavin deficiency. Other workers—*e.g.*, AYKROYD *et al.*—have claimed that nicotinic acid deficiency results in a similar syndrome. Furthermore, the findings of Verzer and his co-workers on the rôle of the adrenals in riboflavin metabolism await confirmation.

Nevertheless, the aetiology of pellagra and its associated syndromes is a problem still requiring an unequivocal explanation, for recent improvements in methods of nicotinic acid assay of foodstuffs are resulting in data which do not appear to strengthen the arguments favouring the notion that pellagra is a consequence of a simple dietary deficiency. The idea that exogenous or endogenous inhibitory factors may play a part in the causation of the condition accordingly deserves consideration. The publication therefore of Dr. Clark's plausible theory, even if it does not result in its immediate acceptance, should fulfil a useful purpose in stimulating further enquiry along the lines suggested by its author.

A misprint appears in the list of the riboflavin content of foodstuffs extracted from FIXSEN and ROSCOE's tables. The figures should read mgm. per 100 gm. not per 500 gm. as printed.]

L. J. Davis.

MALARIA.

Précis of Abstracts in this Section.

Brown (p. 409) discusses the deaths due to malaria in Georgia, U.S.A., during 1937, giving details of 101 patients certified as having died from this disease. He emphasizes the importance of expert diagnosis. Pinotti (p. 409) states that almost one-third of the population of Brazil are infected, and malaria as a cause of death is surpassed only by tuberculosis and intestinal diseases. He refers to the introduction of *A. gambiae* from West Africa.

Gill (p. 410) refers to the vital statistics, which are remarkably good, of Ceylon, in relation to the influence of malaria upon natality. On the basis of spleen rates the island can be divided into five zones, and the death rates and infant mortality rates appear to reflect the baneful effects of malaria. Endemic and epidemic malaria have little influence on natality but increase the frequency of stillbirths. High degrees of immunity confer partial protection against these accidents of pregnancy.

Boyd (p. 411) records observations on patients undergoing therapy with quartan malaria. These cannot be further abstracted, but it is noted that one patient died of the disease after having shown, on one occasion, the high parasite density of 114,000 per cmm. As a rule the parasite densities seen were relatively low.

Dulaney and Stratman-Thomas (p. 411) have prepared antigens, for complement fixation reactions in human malaria, from *P. knowlesi*, *P. vivax* and *P. malariae*. These give strong group reactions but do not cause skin reactions. The complement fixation reactions are strongly correlated with the presence of parasites in the blood, but negative reactions cannot be taken as certain indications of the absence of parasites. The test may be useful in *P. falciparum* infections when parasites, though present in the body, are absent from the peripheral blood.

Taliaferro and Klüver (p. 412) have studied *P. brasilianum* infections in monkeys; they consider that lymphoid hyperplasia in malaria augments the mesenchymal reserve from which monocytes and newly formed macrophages arise.

Huff (p. 413) discusses the size, variability and growth rates of oöcysts of different strains of avian malaria parasites.

As a result of experiments in which sporozoites of *P. gallinaceum* were inoculated into chicks, Shortt *et al.* (p. 413) conclude that the sporozoites are taken up by the endothelial cells, where they multiply by schizogony and increase in number until merozoites enter the red cells. Exoerythrocytic schizogony continues as a low-grade infection and this may be responsible for those cases of malaria in which gametocytes are the only blood forms present. Lumsden and Bertram (p. 414) have studied the biology of *P. gallinaceum* in fowls; the asexual cycle is one of 36 hours and gametocytes appear in the blood at the time when asexual forms are first seen.

To and Cho (p. 414) find that the hydro-derivatives of cinchona alkaloids, though more toxic than the basic substances, are effective in much smaller doses in avian malaria, but in comment Wenyon notes that the observations do not agree with those of other workers.

Lumsden and Bertram (p. 414) have investigated the action of plasmoquine and praequine, in various doses, on the development of gametocytes of *P. gallinaceum* in fowls. Africa *et al.* (p. 415) report on prontosil in avian malaria. *C. W.*

Brown (H. W.). **The Problem of Malaria Mortality.**—*Amer. Jl. Public Health.* 1940. Oct. Vol. 30. No. 10. pp. 1190–1205. With 1 fig.

Malaria is certified as the cause of from 2,500 to 4,500 deaths a year in the United States. With the object of obtaining information regarding the circumstances in which these deaths occur the author sent questionaries to Georgia physicians who certified malaria as the cause of death of patients during the summer and autumn of 1937. Information concerning 101 such patients was obtained, 53 white and 48 coloured. The greatest number of deaths occurred in children under 5 years and in adults past middle age ; the lowest number in the 5 to 9 and 10 to 14 age groups. Half the whites and three-quarters of the negroes had been ill a week or longer before seeking medical aid. Ten per cent. died the day the physician was first called, and 28 per cent. died within the next two days. Thirty-four per cent. of the whites and 8 per cent. of the negroes summoned a doctor during the first two days of illness. Sixty-seven per cent. of these patients took some form of anti-malaria treatment before calling a doctor. Fourteen persons died a month or longer after seeking medical advice. Quinine was the doctor's drug of first choice in treating these patients ; atebrin came next. Forty per cent. did not receive what international authority considers to be adequate treatment to control a severe attack of malaria. Blood smears were made in only 52 of the 101 cases ; parasites were found in 47. *P. falciparum* was found in 23 films, *P. vivax* in 20, both together in one, *P. malariae* in two and an unspecified parasite in one. The large proportion of *P. vivax* infections probably indicates diagnostic error, since *P. vivax* seldom causes death except in the very young or old.

Further education of members of the medical profession in the diagnosis and treatment of malaria is necessary, and further facilities should be provided for the expert examination of blood films.

Norman White.

Pinotti (Mário). O problema da malária do Brasil e a sua invasão pelo *A. gambiae*. [**Problem of Malaria in Brazil and the Invasion of Brazil by** *A. gambiae*.]—*Arquivos de Higiene.* Rio de Janeiro. 1940. June. Vol. 10. No. 1. pp. 127–160. With 10 figs. & 1 graph.

Malaria is an important cause of morbidity in Brazil. Only one of the 21 States, Rio Grande do Sul, appears to be free from the disease. It is estimated that nearly a third of the rural population of 27,000,000 are infected. As a cause of mortality malaria is surpassed only by tuberculosis and intestinal diseases. The author describes the topography and the health conditions of the *Baixada Fluminense*, an area of some 17,000 square kilometres in the Paraiba Valley, including the eastern and part of the southern coastal areas of the State of Rio de Janeiro. An account is given of the large amount of sanitary engineering that has been carried out during recent years and the results

achieved thereby. Fifteen species of anophelines have been found: the most important vector is *A. albitarsis*. *A. darlingi*, *A. argyritarsis* and *A. tarsimaculatus* likewise transmit the disease.

With regard to the introduction of *A. gambiae* into Brazil from Africa no original observations are recorded, but the considerable literature on this important subject is summarized and discussed.

N. W.

GILL (C. A.). **The Influence of Malaria on Natality with Special Reference to Ceylon.**—*Jl. Malaria Inst. of India.* 1940. Sept. Vol. 3. Nos. 2 & 3. pp. 201–252. With 2 maps & 8 graphs. [14 refs.]

This is an epidemiological and statistical investigation into the effects of endemic and epidemic malaria on natality. Under the term "natality" the author includes not only live births, but stillbirths, miscarriages and abortions, or "missed births," as well. He also takes count of "missed conceptions." There are very few tropical or subtropical countries in which the recording of vital and demographic statistics is sufficiently complete to serve as the basis of an investigation of this nature. Ceylon appears to be an exception and the major part of this inquiry is based on the vital statistics of Ceylon for the period 1921-1930. In 1921 and 1922 the spleen rate of all accessible towns and villages in the island was determined: on the basis of this survey the island can be divided into five well-defined zones according to the intensity of endemic malaria prevailing therein. These "iso-splenic" zones are those in which the spleen rate varied from 0–5, 5–10, 10–40, 40–60 and above 60 per cent., respectively. The vital statistics of these zones are compared, corrections being made for variations in the age and sex distribution of the populations. The death rates and the infant mortality rates appear to reflect the baneful effects of malaria. It appears that endemic and hyperendemic malaria exercise no appreciable influence on the birth rate of the indigenous population. Endemic malaria, however, causes a change in the monthly distribution of births, the amplitude of which varies with the intensity of the malaria. Epidemic malaria causes a temporary reduction of the birth-rate, in proportion to its intensity, and a temporary change in the monthly distribution of births. Endemic and epidemic malaria increase the frequency of stillbirths and "missed" births; it is inferred that high degrees of immunity confer partial protection against these accidents of pregnancy.

These are some of the chief conclusions of an investigation that does not lend itself readily to summary.

N. W.

GUINDY: REPORT OF THE KING INSTITUTE FOR YEAR ENDING 30TH SEPT., 1939. pp. 45–48.—**Malaria Investigation—King Institute** [RUSSELL (Paul F.)].

The malaria research activities of the King Institute, Madras, are financed by the Rockefeller Foundation and are under the direction of P. F. Russell. The field investigations of medical, entomological, agricultural and engineering problems of malaria have been carried out in the Pattukkottai taluk, Tanjore, Southern Madras. The results of many of these enquiries have been published in the *Journal of the Malaria Institute of India*, and have been summarized in this *Bulletin*.

N. W.

Boyd (Mark F.). **Observations on Naturally and Artificially Induced Quartan Malaria.**—*Amer. Jl. Trop. Med.* 1940. Nov. Vol. 20. No. 6. pp. 749–798. With 5 figs.

This paper contains a very comprehensive analysis of observations made on 43 patients subjected to malaria therapy with *P. malariae*. Three strains of the parasite were used; they came from widely separated localities but no observations were made to determine their antigenic relationship. In five patients infection was naturally induced; in 43 patients trophozoites were inoculated intravenously. In naturally inoculated cases the incubation period varied between 4 and 5 weeks: parasites were detected in the blood from three to twelve days before the clinical onset. In artificially induced infections the mean interval between inoculation and the first detection of parasites was 9·5 days, and between inoculation and the clinical onset 19·2 days. The mean duration of naturally induced attacks, regardless of therapeutic interference, was 132 days, and of artificially induced attacks 92 days. Early paroxysms were always simple quartan in type: double quartans and quotidian fevers were only seen in advanced stages of the attack. An onset with remittent fever was rarely seen. Paroxysms after artificial inoculation show greater complexity and irregularity than those following natural infections. The parasite densities observed were considerably lower than those commonly observed in *P. falciparum* and *P. vivax* infections. In one very exceptional case of the series, however, a parasite density as high as 114,000 per cmm. was observed on one occasion; this patient died, apparently of malaria, in spite of heavy doses of quinine. In the two other cases that terminated fatally malaria does not appear to have been responsible for death.

But little justice can be done to this exhaustive study within the scope of a summary. *N. W.*

i. Dulaney (Anna Dean) & Stratman-Thomas (Warren K.). **Complement Fixation in Human Malaria. I. Results obtained with Various Antigens.**—*Jl. Immunology.* 1940. Sept. Vol. 39. No. 3. pp. 247–255. With 1 fig.

ii. Stratman-Thomas (Warren K.) & Dulaney (Anna Dean). **Complement Fixation in Human Malaria. II. Diagnostic Application.**—*Ibid.* pp. 257–264.

i. By means of an antigen prepared from *Plasmodium knowlesi* parasites collected by centrifugation from laked red blood corpuscles of infected monkeys, complement fixation tests have been carried out. The parasites, washed free of haemoglobin, are dried *in vacuo* and ground to powder in a mortar. For use 0·1 gm. of the powder is ground in a mortar with 10 cc. of saline. The solution is then frozen and thawed four times with a dry ice-alcohol mixture. The liquid is then centrifuged, the supernatant fluid being standardized against known positive and negative malarial sera and tested for anticomplementary properties. Similar antigens have been prepared from *P. vivax* and *P. malariae*. With these antigens strong complement fixation was obtained with sera from cases of any of the three malarial infections. The reaction is thus a group rather than a specific one. Pre-existing syphilis has not been found to modify the reaction. A Wassermann-negative patient may still give a negative Wassermann reaction at a

time when malarial parasites are present in his blood and a 4 + malarial complement fixation has been obtained. Attempts to obtain cutaneous or precipitative reactions specific for malaria were not successful, nor did antigens prepared by other methods yield as definite results as the one employed.

ii. In the second paper it is shown that complement fixation tests in malaria are very closely correlated with the presence of malarial parasites in the peripheral blood. A strongly positive reaction means the presence or recent presence of parasites in the blood. A negative reaction cannot, however, be taken as a certain indication of the absence of parasites. With increase in the number of parasites in the blood the intensity of the reaction increases also. From the standpoint of diagnosis the reaction might be of value in *P. falciparum* infections when parasites, though present in the body, are absent from the peripheral blood. *C. M. Wenyon.*

DULANEY (Anna Dean) & STRATMAN-THOMAS (Warren K.). **Specific Nature of Complement Fixing Antibody in Malaria as demonstrated by Absorption Tests.**—*Proc. Soc. Experim. Biol. & Med.* 1940. June. Vol. 44. No. 2. pp. 347–349.

The authors have confirmed the results of COGGESHALL and EATON that a specific complement fixation reaction in malaria employing *Plasmodium knowlesi* antigen can be obtained. A positive reaction is correlated with the presence or recent presence of demonstrable parasites in the blood. It has also been shown that Wassermann negative patients who receive induced malarial infections remain Wassermann negative, though they become malaria positive. Absorption experiments carried out on bloods which are both Wassermann and malaria positive indicate that each reaction depends upon distinct and correlated antigens. *C. M. W.*

TALIAFERRO (William H.) & KLÜVER (Cessa). **The Hematology of Malaria** (*Plasmodium brasilianum*) **in Panamanian Monkeys. 1. Numerical Changes in Leucocytes.**—*Jl. Infect. Dis.* 1940. Sept.–Oct. Vol. 67. No. 2. pp. 121–161. With 9 figs. [101 refs.]

—— & ——. **The Hematology of Malaria** (*Plasmodium brasilianum*) **in Panamanian Monkeys. 2. Morphology of Leucocytes and Origin of Monocytes and Macrophages.**—*Ibid.* pp. 162–176. With 2 coloured plates. [22 refs.]

These papers describe observations on the blood cells of a number of Central American monkeys both before and after infection with *Plasmodium brasilianum*, a parasite with a quartan periodicity. The cells were studied from the point of view of quantitative as well as qualitative changes, while the sacrifice of a number of the animals at selected stages of their malarial infections enabled the changes in the blood to be compared with those in the spleen, liver and bone marrow. In two coloured plates the various cells as seen in the blood and in the organs are depicted. The general results of this study are in agreement with those of previous investigations. They afford further evidence in support of the view that the lymphoid hyperplasia in malaria augments the mesenchymal reserve from which monocytes and newly formed macrophages arise. *C. M. W.*

Huff (Clay G.). **Quantitative Studies on Size, Variability, and Growth Rates of Oöcysts of Different Strains of Avian Malaria.**—*Amer. Jl. Hyg.* 1940. Nov. Vol. 32. No. 3. Sect. C. pp. 71–80. With 2 figs. [15 refs.]

The author describes observations on the infectiveness and rate and extent of growth of oöcysts in mosquitoes (*Culex pipiens*) of two strains of *Plasmodium cathemerium* and one of *P. relictum*. One strain of *P. cathemerium* differed from the other in its greater infectiveness for mosquitoes and in the greater maximum size of the oöcysts. There were significant differences in size of the oöcysts in any individual mosquito, but these were not so great as those in different mosquitoes. The rate of growth of oöcysts decreases progressively as they approach their maximum size. *C. M. W.*

Shortt (H. E.), Menon (K. P.) & Iyer (P. V. Seetharama). **The Form of *Plasmodium gallinaceum* Present in the Incubation Period of the Infection.**—*Indian Jl. Med. Res.* 1940. July. Vol. 28. No. 1. pp. 273–276.

The authors have attempted to obtain evidence that the exoerythrocytic schizonts in the fowl malarial parasite *Plasmodium gallinaceum* are the forms which develop directly from sporozoites, by inoculating with sporozoites very young chicks or chicks still within the egg. Sporozoites from the salivary glands of mosquitoes were deposited on the chorio-allantoic membrane of a 13-day-old chick embryo. Eleven days later the chick had made a hole in the eggshell but had failed to escape. It was found to be dead. On examination a very intense infection of the brain capillaries with exoerythrocytic schizonts was found. Smears of the heart blood showed only a moderate infection of red blood corpuscles with pigmented parasites. In a second experiment sporozoites were inoculated intramuscularly into a three-weeks-old chick. Seven days later the chick was sacrificed. It was found to be in very much the same condition as the first chick, except that the erythrocytic forms in smears of heart blood were too young to show pigment. As in the case of the first chick, the extent of the brain infection with exoerythrocytic forms must have been the result of several days' development. In a third experiment a chick about three weeks old was inoculated intramuscularly with sporozoites. Six days later it was sacrificed. Only a scanty infection of the brain with exoerythrocytic schizonts was found, while no erythrocytic forms could be found in the blood. The same result was obtained when the experiment was repeated. The authors interpret these results as follows. The sporozoites enter the blood and are taken up by or actively enter the endothelial cells lining the blood capillaries and other endothelial cells. They multiply by schizogony and increase in number till merozoites enter red blood corpuscles to become the pigmented forms. The exoerythrocytic schizogony continues as a low-grade infection which is not visually detectable till it is stimulated to further development and causes a relapse of the pigmented blood forms. It has generally been assumed that malaria persists as a low grade infection with pigmented forms but the authors think that such an assumption is unnecessary. It may be merozoites from exoerythrocytic schizonts which are responsible for cases of malarial infection in which gametocytes are the only blood forms present. It is perhaps of interest to note that the strain of *P. gallinaceum* used is not the one

brought to Europe by BRUMPT and now distributed in many laboratories, but another one from the same source in Ceylon which was sent to Guindy, Madras, where the work was carried out. *C. M. W.*

LUMSDEN (W. H. R.) & BERTRAM (D. S.). **Observations on the Biology of *Plasmodium gallinaceum* Brumpt, 1935, in the Domestic Fowl, with Special Reference to the Production of Gametocytes and their Development in *Aëdes aegypti* (L.).**—*Ann. Trop. Med. & Parasit.* 1940. Sept. 26. Vol. 34. No. 2. pp. 135–160. With 6 figs. [28 refs.]

The authors have studied *Plasmodium gallinaceum* as it develops in 12–16-weeks-old fowls infected either by intramuscular or intravenous inoculations of blood or by the bites of infected *Aëdes aegypti*. This has involved daily observations on the blood in order to determine the average length of the incubation or prepatent period, the intensity of the infections, the variations in ratio of asexual to sexual forms, the periodicity of the asexual cycle and the number of gametocytes present and their infectivity to mosquitoes as judged by the number of oöcysts developing on the stomach. The observation of GIAVANNOLA that the asexual cycle is one of 36 hours was confirmed, the maximum schizogony occurring at midnight and midday alternately. It was noted that gametocytes infective to mosquitoes appeared in the blood at the commencement of the patent period, when asexual forms first became evident. The results obtained are compared with those of other observers on other species of malarial parasite. For a complete comprehension of the subject the paper is one which must be read in its entirety. *C. M. W.*

TO (Somei) & CHO (Shoren). Vergleichende Untersuchung ueber die Wirkung der Chinaalkaloide und deren Hydro-Derivate auf die Malaria des Vogels. [**Comparison of the Action of the Cinchona Alkaloids and their Hydro-Derivatives on Bird Malaria.**]—*Taiwan Igakkai Zassi* (*Jl. Med. Assoc. Formosa*). 1940. Aug. Vol. 39. No. 8. [In Japanese pp. 1378–1391. [10 refs.] German summary pp. 1391–1393.]

The authors have investigated the toxicity and plasmodicidal activity of quinine, quinidine and cinchonine and their corresponding hydro-derivatives on bird malaria. Though the hydro-derivatives are more toxic than the basic substances they are therapeutically effective at half their lethal doses. It is concluded that the hydro-derivatives being effective in doses so far removed from the lethal dose should be more useful for the treatment of malaria than the basic substances themselves. [Investigations carried out by BUTTLE, HENRY and TREVAN (1934) gave results which do not agree with those recorded in the paper reviewed (this *Bulletin*, 1934, Vol. 31, p. 699).] *C. M. W.*

LUMSDEN (W. H. R.) & BERTRAM (D. S.). **The Effect of Plasmoquine and of Praequine on the Subsequent Development of the Gametocytes of *Plasmodium gallinaceum* Brumpt, 1935, in *Aëdes aegypti* (L.).**—*Ann. Trop. Med. & Parasit.* 1940. Sept. 26. Vol. 34. No. 2. pp. 161–172. With 3 figs. [19 refs.]

Experiments are described in which the influence of plasmoquine and praequine (the French equivalent of plasmoquine) have been

tested on gametocytes of *Plasmodium gallinaceum*. Fowls were infected by mosquito bites and when parasites appeared in the blood single doses of one or other drug were given by oesophageal tube into the crop. The infectivity of the gametocytes to mosquitoes (*Aëdes aegypti*) was tested by feeding mosquitoes on the fowls at varying intervals of time. A dose of plasmoquine of 15 mgm. per kilo. of body-weight produced rapid diminution of the general infection, which persisted, however, for five days. No mosquitoes were infected after 46 hours from the dose. In a dose of 2·6 mgm. per kilo. plasmoquine has no obvious effect on the general infection, but mosquitoes fed 4 and 22 hours after the dose failed to become infected. Plasmoquine and praequine in a dose of 1·4 mgm. per kilo. orally had no effect on the general infection, while mosquitoes were still infected after 12 hours. Both these drugs in a dose of 0·14 mgm. had no effect on the general infection, while massive infections were still produced in mosquitoes 16 hours after the administration of the drugs. There appears to be no difference in the action of the two drugs.

C. M. W.

Africa (Candido M.), Dy (Francisco J.) & Soriano (Lily J.). **Studies on the Effect of Prontosil on Avian Malaria : a Preliminary Report.** —*Acta Med. Philippina.* Manila. 1939. July–Sept. Vol. 1. No. 1. pp. 19–26.

The authors have treated bird malaria (*Plasmodium relictum* in *Padda oryzivora*) by a varying number of intramuscular injections of prontosil. In nine birds which survived the treatment all parasites disappeared from the blood at the end of the course, whereas in a number of control untreated birds the parasites persisted.

C. M. W.

MISCELLANEOUS.

Manson-Bahr (Philip). **The Prevalent Diseases of Libya.**—*Lancet.* 1941. Feb. 22. pp. 253–255. With 3 figs. [13 refs.]

This paper cannot be abstracted, but attention is drawn to it here on account of its value to those who may find themselves in N. Africa. The prevalent diseases are mentioned, and the author gives not only the findings of other workers, but also the results of his own extensive observations on these conditions as they affected troops in N. Africa during the last war, laying stress not so much on the classical appearances as on those features which might confuse medical officers not accustomed to dealing with the disease in question. He deals with malaria, especially subtertian, which is prevalent in the Fezzan, leishmaniasis, relapsing fever, typhus, sandfly and dengue fevers, deficiency diseases, dysentery, helminthic diseases, venereal diseases and desert sore. The common venomous animals are referred to. Modern lines of treatment are indicated. The paper is concise but is full of essential information ; it should be available for reference to every medical officer working in N. Africa. *C. W.*

SMITHBURN (K. C.), MAHAFFY (A. F.) & PAUL (J. H.). **Bwamba Fever and its Causative Virus.**—*Amer. Jl. Trop. Med.* 1941. Jan. Vol. 21. No. 1. pp. 75–90.

This is the second virus discovered in Uganda in the course of attempts to isolate the yellow fever virus by the group of workers from the Rockefeller Foundation. The fever occurred in a group of labourers constructing a road through Bwamba county, which is approximately 18 miles long by 9 miles wide and is in the western Province of Uganda. The main clinical features of the disease were sudden onset of fever, headache and backache which lasted 5 to 7 days. Convalescence was rapid and complete with no fatal cases seen. The virus was isolated from the blood of nine such cases by intracerebral inoculation in mice. The virus caused illness or death when inoculated intracerebrally or intranasally in mice, a fever only when injected intracerebrally in monkeys, and no febrile or clinical reaction in guineapigs.

The lesions produced in mice were limited to the nervous system and characterized by damage to cortical cells in various areas of the brain and by the appearance of intranuclear acidophilic bodies resembling inclusions. Filtration experiments indicate that the size of the virus approximates 113 to 150 mμ.

The serum of convalescent human beings, mice, monkeys and guineapigs all contain neutralizing antibodies to the virus.

F. O. MacCallum.

EARLE (K. Vigors). **Whale Oil as a Local Application in Tropical Ulcer.** —*Jl. Trop. Med. & Hyg.* 1941. Jan. 1. Vol. 44. No. 1. pp. 1–2.

Cod-liver oil as a topical application for the treatment of tropical ulcers has been favourably reported upon, the oil being applied under elastoplast. Its use has, however, the very serious drawback of producing an odour so disgusting that those in the neighbourhood cannot tolerate it. In 1934, DE DZIEMBOWSKI reported favourably on the use of whale oil for dressing burns, wounds, gangrene and the like, adding that it suppressed the foul odours which often are associated with these conditions. The author has now used it for cases of tropical ulcer, his procedure being as follows: The ulcer is first cleaned by several applications of $CuSO_4$ solution or of $MgSO_4$ and glycerin; then an ointment of whale oil 30–40 per cent., with vaseline 70–60 per cent. is smeared on and the site bandaged with elastoplast. This is left untouched for 10–14 days during which the patient is instructed to rest. Details are given of four patients, with ulcers associated with Vincent's spirochaete, in all of whom healing was complete in 3–4 weeks. All four were also given one of the sulphonamide group of drugs.

H. H. S.

HARVEY (W. F.). **Studies in Method and Standardisation of Blood Examination. VII. Blood Sedimentation Rate, Sedimentation Volume and Centrifuge Volume.**—*Edinburgh Med. Jl.* 1941. Jan. Vol. 48. No. 1. pp. 14–25.

For these examinations the author uses common vaccine lymph tubes of 1 mm. bore, and points out that, within limits, the bore does not greatly influence the result, but that it is essential that

the bore should be uniform throughout each tube. The tubes are thrown away after use so that elaborate cleaning is dispensed with. Blood from a finger prick is satisfactory.

Technical details are given: 4 drops of blood are diluted with 1 drop of 3·8 per cent. citrate solution and this mixture is taken up into the tubes to a height of 5 cm. Sedimentation readings are taken at 20 minutes, 1 hour and 24 hours, and after this the tubes are centrifuged and the height of the column of packed cells is measured. It was found that there was a fairly constant relation between the height of the column of red cells after sedimentation for 24 hours and the height after centrifugation. The factor was 0·75 which, when multiplied by the former observation, gave value of the latter. But these readings, of course, are in blood diluted with citrate solution; for undiluted blood allowance for the citrate must be made. Nevertheless the author considers that when a centrifuge is not available, the height of the column of red cells after sedimentation for 24 hours, adjusted by these calculations, is a very useful substitute for the volume of packed red cells or for a red cell count. Dilution may be avoided by using dry powdered oxalate as anticoagulant. [The method may be most useful to workers in the tropics who find difficulty in obtaining laboratory services, or who have not enough practice to undertake with certainty the skilled operation of blood counting.] *C. W.*

LEDERER (Richard). **A New Form of Acute Haemolytic Anaemia "Baghdad Spring Anaemia."**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1941. Mar. 27. Vol. 34. No. 5. pp. 387–394.

Cases of acute anaemia in children occur every year in Baghdad in spring, and some are fatal. In April and May, 1940, the author observed 14 cases, of which one ended fatally. The onset is sudden, with abdominal pains and vomiting. Pallor is immediate and conspicious and jaundice follows in a few hours. After the first stage drowsiness occurs. In severe cases the condition assumes a dangerous appearance in 12 to 18 hours. The red cell count averages 1,000,000 and the white cell count from 18,000 to 45,000. The course is rapid; in the fatal case death occurred in 36 hours, and in those that were cured the anaemia recovered after two weeks. The condition suggested anaphylaxis and a detailed account is given of the investigation which confirmed the theory. Flowers (*Verbena, Mathiola* and cornflower) seem the most likely agents. A similar condition called "favismo" has been described in Sicily and Southern Italy. All the cases were in boys and 13 of the 14 were Jews of a significant constitutional type. The treatment was by the administration of blood, liver extract, and injection of adrenalin. *W. P. Kennedy.*

WIGGLESWORTH (V. B.). **The Sensory Physiology of the Human Louse *Pediculus humanus corporis* de Geer (Anoplura).**—*Parasitology.* 1941. Mar. Vol. 33. No. 1. pp. 67–109. With 35 figs. [41 refs.]

This paper describes the sense organs of the louse, the sensory responses, and the mechanisms of orientation to various stimuli. The antennae bear tactile hairs, some thin-walled cones at the apex

which are shown to be organs of smell and some delicate tufts shown to be humidity receptors. The temperature sense occurs on the antennae and elsewhere on the body. The structure of the eyes is described. The sensory responses are studied mainly by observing the track of the louse in an arena in which the two halves differ in a single stimulus at a time. "Temperatures above or below 31°–29°C. are avoided; high humidities are avoided—though this response is readily influenced by the experience of the louse in the immediate past, and by exposure to high humidities it may be caused to avoid low; the smell of human clothing or other lice or their excreta are all attractive; almost any odorous chemical is repellent; smooth materials are avoided if rough materials have been recently experienced. Light is avoided.

The response to light is mainly a "directed response": the louse is orientated toward an area of shade. The responses to temperature, smell, humidity and contact are mainly "undirected responses": when moving in a favourable zone the louse follows a straight course; on entering an adverse zone (or a zone where some favourable stimulus recently experienced is absent) it follows a convoluted track. Thus the louse, turning when the intensity of stimulus falls, keeping straight while the stimulus remains constant or increases, gradually finds its way to the centre of a favourable zone. *V. B. Wigglesworth.*

KELSEY (A. J.). **Larva Migrans or Myiasis Linearis treated by Diathermy.**—*Med. Jl. Australia.* 1940. Oct. 19. 27th Year. Vol. 2. No. 16. p. 379. With 2 figs.

[Creeping eruption, the condition due to *Larva migrans*, has several causes, among them the larval nematode of *Ancylostoma braziliense*, in Ceylon and S. Africa, or a mite allied to *Tetranychus molestissimus*, in the Argentine and Uruguay, *Hypoderma*, *Gastrophilus haemorrhoidalis* in Russia, *Uncinaria stenocephala* and *A. caninum* (experimentally in volunteers) as stated in Manson-Bahr's *Manson's Tropical Diseases*.

In the present case the actual cause is not stated, the interest of the record lying in the results of treatment. Hitherto treatment has not been very satisfactory. Injection of cocaine and parasiticides in front of the advancing larva may be quite ineffectual, ethyl acetate on collodion flexile *may* cure; refrigeration with ethyl chloride gives better, but not certain, results; carbon dioxide snow causes much pain, and may set up a secondary dermatitis, refractory to treatment; local inunction of oil of chenopodium has given good results in some cases.]

The patient showed an extensive area of involvement—the back and front of the right shoulder and axilla—the condition had persisted for two months. The length of the burrows might run to 2 feet, and the rate of advance was about an inch daily. There was a pustular dermatitis from secondary infection due to irritation and scratching. Ethyl chloride was ineffectual. The author used the needle point of a diathermy apparatus, with a 1/16 inch spark and if the spark was directed to the right spot relief was immediate; there were some 25 burrows and probably more. Treatment was given for seven days, and, judging by photographs showing the condition on the second and eighth days of treatment, the result left nothing to be desired. [See also this *Bulletin*, 1940, Vol. 37, p. 534.] *H. H. S.*

COTTERELL (G. S.). **Preliminary Investigations on the Fly Population of Stable Manure Heaps and Measures for the Prevention of Breeding.**—*Pap. 3rd W. Afr. Agric. Conf. Nigeria June 1938 Sect. Gold Coast.* Lagos. [1940]. Vol. 1. pp. 118–125. With 2 plates. [Summarized in *Rev. Applied Entom.* Ser. B. 1941. Mar. Vol. 29. Pt. 3. pp. 46–47.]

"As mixed farming, including the keeping of cattle, is being advocated in the Gold Coast, experiments were carried out to ascertain to what degree Muscoid flies breed in manure heaps and in which parts of the heaps breeding occurs, the effects of fermentation, and the extent to which breeding might take place in droppings in the field. Nearly all the Muscoids found were *Musca domestica*, L., or other Muscids, most of which, it is thought, will prove to be small examples of this species, which are often bred from drying material and cannot reproduce. An investigation of an old existing dump consisting chiefly of horse manure and bedding stacked on a concrete floor and surrounded by concrete walls on three sides showed that breeding of *M. domestica* was inhibited where the temperature of the manure was high owing to fermentation, and occurred chiefly in the surface layers. It also appeared that larvae were constantly being added to the heap with fresh manure. As this dump was not considered typical, further observations were made on a heap of cattle manure stacked on a beaten earth floor under cover and prepared over a period of three weeks. All but one of the 184 larvae and pupae taken in it were in the surface samples, which were taken from a depth of 3 ins. only and in which the temperature was less than 50°C. [122°F.]. It was also shown that the larvae could pupate successfully in the hard beaten earth under, and particularly at the immediate edge of, the heap. Extensive breeding was found to take place in the field in cattle dung 1–3 days old and a certain amount in dung less than 24 hours old. More flies were produced per cubic foot from dung 1–3 days old than in any part of the dung heap under observation. Two experiments were carried out to test the possibility of flies breeding in heaps of cattle dung in which fermentation is complete. The heaps were caged for 18 or 19 days to allow flies to emerge; they were then re-exposed for 5 days, after which they were caged again and emergence once more observed. In one experiment, 276 Muscids emerged during the first period and 282 during the second, but in the other, only one fly (*Stomoxys* sp.) appeared during the second period, though 583 Muscids emerged during the first.

"Previous workers have ascertained that house-flies cannot live in manure with a temperature of 114·8°F. In the present observations, temperatures as low as this were recorded only in the immediate surface layer and in manure in which fermentation was complete. It is therefore suggested that breeding may be restricted to some extent if the depth of the cooler surface layer is reduced by close packing each time fresh manure is added. In dry weather, it may be necessary to sprinkle a little water on the heap before it is beaten down. Breeding can also be considerably reduced by covering heaps with oiled Hessian cloth. In an experiment with two identical heaps, the covered and uncovered ones produced, respectively, 66 and 276 flies. To prevent infestation of dwelling houses, cattle should not be allowed to graze within 700–800 yards of them unless all dung is collected daily."

LENNOX (F. G.) & WEBBER (L. G.). **Studies of the Physiology and Toxicology of Blowflies. 3. The Toxicity of Some Arsenicals to Larvae of *Lucilia cuprina*.—*Commonwealth of Australia. Council for Scientific and Industrial Research. Pamphlet No. 101.* Melbourne. 1940. pp. 51–67. With 1 fig. [15 refs.]

" By incorporating several well-known arsenicals in a synthetic medium and feeding them to *L. cuprina* larvae, their relative toxicities to this organism were assessed. As a measure of toxicity the percentage mortality was recorded for each poison at frequent intervals during the course of the experiment, and, from the resultant time-mortality curves, times for 50 per cent. mortality were read.

" Although the compounds were compared both at equal percentage concentrations and at equivalent arsenic concentrations, there was no major difference between the relative order within the two series. Thus, it was not possible to correlate the toxicity of a compound with its total arsenic content. However, there was some correlation between toxicity and arsenic dissolved by the enriched medium.

" The results show that the arsenicals could be subdivided into two groups. Firstly, the highly toxic compounds comprising, in order of decreasing toxicity, barium arsenite, calcium arsenite, arsenic acid, Paris green, and arsenious oxide ; and secondly, the moderately toxic arsenates of zinc, aluminium, lead, and calcium.

" The absence of pigment from the crops or guts of larvae on stained enriched medium, containing toxic concentrations of sodium or calcium arsenite, is taken to indicate that these arsenicals may not destroy the larvae through absorption of arsenic from the gut."

LENNOX (F. G.). **Studies of the Physiology and Toxicology of Blowflies. 4. The Action of Contact Larvicides on *Lucilia cuprina*.—*Commonwealth of Australia. Council for Scientific and Industrial Research. Pamphlet No. 101.* Melbourne. 1940. pp. 69–131. With 18 figs. [65 refs.]

" A method is described for measuring the contact toxicities of liquids to *L. cuprina* larvae by totally immersing a constant number of prepupae in the test liquid under standard conditions and determining the percentage which is unable to complete metamorphosis.

" Using this method the influence of concentration, time of contact, and temperature, on the toxicity of a poison are studied. The concentration-mortality curves for acetone, ethyl acetate, and acetic acid, each diluted with water, methyl alcohol, and ethyl alcohol, show that the steep inflexion of the typical sigmoid curve is displaced towards the less toxic component by increase in toxicity of either component.

" Owing to the difficulty of administering very small doses of the undiluted liquids, the time-mortality curves rise sharply during the first few minutes, and this rise becomes more acute with increase in the toxicity of the test liquid. In fact, substitution of a highly toxic for a slightly toxic liquid, increase in the concentration of acetic acid, or increase in the temperature of acetone, diminishes the length of the initial horizontal portion of the sigmoid curve.

" A semi-logarithmic relationship exists between the time for 50 per cent. mortality of *L. cuprina* and the concentration of acetic acid or the temperature of acetone. Calculation of the temperature coefficients for acetone gives values of the same order of magnitude as previously recorded for the action of various chemicals on bacteria.

" A type of drug antagonism, which operates when small amounts of toxic liquids are added to practically non-toxic liquids, is noticeable, particularly when inhibition of pupation rather than fly emergence is used to measure mortality. The choice of one or other of these two criteria may have a considerable influence on the apparent relative toxicities of two compounds, because they do not always bear the same constant relationship to each other.

" The contact toxicities of hydrochloric acid and sodium hydroxide are approximately equal, and greater than those of weaker acid and alkali. It is highly probable that the toxicities of inorganic acids and alkalis are a direct function of their hydrogen ion and hydroxyl ion concentrations respectively.

" Measurements of the toxicities of a wide variety of pure liquid organic chemicals show that aliphatic halogenated and aromatic hydrocarbons are exceptionally potent, and in the normal aliphatic alcohols or fatty acids toxicity increases as the carbon chain lengthens within the homologous series. Isomers of alcohols or acids are less toxic than the corresponding normal compounds. Aqueous solutions of the free base, nicotine, are considerably more toxic than solutions containing nicotine as sulphate. Amongst the most toxic of the essential oils are caraway, dill, mustard, origani, and thyme. Tests with coal tar fractions show that their toxicities increase with volatility and tar acid content. Lipoid solvents are exceptionally toxic to *L. cuprina*, and it is considered that they act by dissolving the outermost cuticular layer thereby facilitating penetration of the cuticle."

Roy (A. C.), Mazumdar (D. C.) & Mukherjee (P.). **The Anti-Haemolytic Action of 'Soluseptasine': a Drug belonging to the Sulphanilamide Group.**—*Indian Jl. Med. Res.* 1940. July. Vol. 28. No. 1. pp. 235–240.

The mode of action of drugs of the sulphanilamide group is still obscure and the authors, who have been investigating the haemolytic properties of certain substances, have tested the effect of a drug of this group on the haemolytic power of cobra venom, bile salts, saponin, cyclamin, and of the supernatant fluid from centrifuged 18-hour fluid cultures of the El Tor vibrio and a haemolytic streptococcus. On the haemolytic action of all these, soluseptasine was found to have a definite retarding action. On sodium oleate the action was irregular. Protocols of the controlled experiments are given but cannot be reproduced in detail here. *C. W.*

de Waal (H. L.). **South African Senecio Alkaloids.** [Correspondence.]—*Nature.* 1940. Dec. 14. Vol. 146. No. 3711. pp. 777–778. [Summary appears also in *Bulletin of Hygiene.*]

From *Senecio retrorsus* the alkaloid retrorsine has been isolated; it has the formula $C_{18}H_{25}O_6N$. The author has also isolated isatidine, $C_{18}H_{25}O_7N$, and another alkaloid whose formula may be $C_{18}H_{25}O_8N$. Both the latter are soluble in water but not in chloroform. From *Senecio rosmarinifolius* a new alkaloid, rosmarinecine, has been isolated with formula $C_{18}H_{27}O_6$, and on hydrolysis yields senecic acid and a base rosmarinecine. *Senecio pterophorus* contains retrorsine and a new alkaloid pterophine, $C_{18}H_{23}O_5N$.

In the " bread poisoning " which affects human beings in the Cape south-western districts of South Africa, it is the *Senecio ilicifolius*

which is responsible. This contains the above-mentioned retrosine and pterophine and a third alkaloid, senecionine. A fuller report on the investigation is to appear later. [Senecio poisoning was first described in South Africa in 1918. See *Bull. of Hyg.*, 1936, Vol. 11, p. 849; 1937, Vol. 12, p. 898, and this *Bulletin*, 1921, Vol. 17, pp. 250–252.] *H. H. S.*

DOBELL (Clifford). **Researches on the Intestinal Protozoa of Monkeys and Man. X. The Life-History of *Dientamoeba fragilis*: Observations, Experiments, and Speculations.**—*Parasitology.* 1940. Nov. Vol. 32. No. 4. pp. 417–461. With 65 figs. on 2 plates & 1 text fig. [66 refs.]

This, the tenth contribution by the author on the subject of the intestinal protozoa of monkeys and man, deals with that enigmatic amoeba *Dientamoeba fragilis*, which was first described by him and Miss JEPPS in 1918. Since the original account the amoeba has been discovered in man in all parts of the world and, in addition, by certain observers in monkeys. The author has studied several strains of the amoeba in cultures and these have shown him that the forms which were first described from faeces must have been degenerate, so that he was misled as to the correct structure. The culture forms can be observed and prepared without any changes of temperature or exposure to unfavourable conditions and it is on these that the present corrected description is based. Several remarkable facts have come to light. In the first place the binucleate condition of the amoeba, in which it is most commonly seen both in faeces and in cultures, is due to an arrest of the nuclear division process in the telophase of mitosis, so that in each half of the dividing nucleus, which retains the nuclear membrane, are a series of chromosomes. There are usually six of these and one is larger than the others. Furthermore the two nuclei are connected by a thread, a centrodesmus (the author prefers this spelling to the more usual centrodesmose) at the point of attachment of which a minute granule is sometimes visible. The author points out that the whole of this arrangement is reminiscent of a flagellate rather than an amoeba and that *D. fragilis* bears a close resemblance to *Histomonas meleagridis*, the cause of blackhead in turkeys, which lives as a flagellate in the caecum of the fowl but which can invade the caecal tissues and liver of turkeys, where it is in an aflagellate amoeboid stage. The division stages of *H. meleagridis* are strikingly like those of *D. fragilis*, in fact the two organisms resemble one another very closely except that the one in certain stages possesses a flagellum while the other, so far as present observations go, never does. It is known that transmission of *H. meleagridis* from host to host is effected by the eggs of an intestinal worm (*Heterakis papillosa*) and it is tentatively suggested that the human parasite *Trichuris trichiura* might play a similar part in the case of *D. fragilis*. In favour of some such method of transmission is the complete absence of encysted stages. Attempts to transmit *D. fragilis* to man and to two macaques *per os* and to the monkey *per anum* failed. A number of chicks were inoculated *per anum* but only in one case was a transitory infection of one week's duration obtained.

The paper, like others of the series, contains a mass of information and detail about the amoeba, if indeed it is an amoeba, the methods of its culture, its habits and structure, while three plates, executed with the author's well-known skill, illustrate all that is known of the

amoeba's morphology and certain features, for purposes of comparison, of *H. meleagridis*. *C. M. Wenyon.*

MASON (Eleanor D.). **The Effect of Change of Residence from Temperate to Tropical Climate on the Basal Metabolism, Weight, Pulse Rate, Blood Pressure, and Mouth Temperature of 21 English and American Women.**—*Amer. Jl. Trop. Med.* 1940. Sept. Vol. 20. No. 5. pp. 669–686. With 6 figs.

"Measurements have been made under basal conditions of weight, pulse, blood pressure, mouth temperature, and metabolism of twelve English and American women changing their residence from temperate to tropical climates (South India). These data are analyzed and compared with a similar study of nine women reported in 1934. For one subject, records are charted covering a period of twelve years, including three furlough periods in America and two 5-year periods in Madras.

"The results found in this series of twelve are consistent with those in the 1934 series. From the combined study of 21 women in the basal state, the following conclusions may be drawn :—

"1. The weight tends to decrease in the tropics.

"2. The pulse rate falls in the tropics in almost all cases, the average of all cases being a fall of 9 per cent., or 6 beats a minute.

"3. There is a trend toward slightly lowered systolic and diastolic pressures, but much individual variation.

"4. The mouth temperature either shows no significant change or rises in the tropics. The average for the whole series is a rise of 0·3°F.

"5. With regard to basal metabolism, two sharply marked types of behaviour appear with the change to tropical climate. Eight, or 38 per cent., of these 21 women, showed no significant change in metabolism. Thirteen, or 62 per cent., showed a distinct fall in metabolic rate in the tropics, averaging approximately 10 per cent. This change, when it occurs, takes place promptly, *i.e.*, within the time required for the journey, and in those few cases studied for longer periods the behaviour has been consistent in the same individuals. It occurs in both newcomers and old residents. When this type of person returns to temperate climates the rate of metabolism rises to its former level, again promptly.

"6. The data suggest strongly a relation between body temperature and metabolic response to the tropics. Both series show a greater rise in temperature in the tropics in those women whose metabolism does not change. Both series also suggest that persons of this type, with constant metabolism but rising temperature, are more likely to have been persons with low body temperatures in temperate climates. Apart from this possible factor, there appears to be no way of predicting from measurements in temperate climates which type of tropical response an individual will show.

"7. There is as yet no real evidence that one type of tropical response is a better adaptation than the other."

MOTTOULLE (Léopold). **Medical Aspects of the Protection of Indigenous Workers in Colonies.**—*Internat. Labour Rev.* 1940. Apr. Vol. 41. No. 4. pp. 361–370.

REED (Alfred C.). **The Future of Tropical Medicine.**—*Amer. Jl. Trop. Med.* 1940. Jan. Vol. 20. No. 1. pp. 1–11. [10 refs.]

REVIEWS AND NOTICES.

CAMERON (Thomas W. M.) [Professor of Parasitology, McGill University, etc.]. **The Parasites of Man in Temperate Climates.**—pp. xi+182. With 61 illustrations. 1940. Toronto, Canada: The University of Toronto Press. [$3.00.]

The purpose of this book is clearly defined in the preface: "It is intended for the medical man who practises in the English-speaking temperate and sub-tropical zones. Only parasites which actually occur in North America or Great Britain are discussed in detail." The book is not intended for students of tropical medicine. The first part deals with protozoa. Of the intestinal protozoa *Entamoeba histolytica* is naturally given prominence, and it is adequately described, with information as to the mode of transmission, pathological effects and treatment. The combined treatment of amoebiasis with emetine bismuth iodide and yatren, however, is not mentioned; yatren is described as the drug of choice but emetine hydrochloride may be used if the liver is invaded or if there is severe abdominal distress. The other intestinal protozoa are adequately described and illustrated in beautifully prepared drawings. Of the trypanosomes only *T. cruzi* is described, but the malaria parasites receive considerable attention.

The parasitic worms are dealt with much more fully. They are described in detail and the transmission of infection, pathological effects, treatment and control are dealt with. Emphasis is placed on Trichinella, the hookworms, the cercariae causing swimmers' itch, and Echinococcus, but a number of other worms are described.

Of the arthropods the genus Dermacentor is given prominence, and of the Diptera the mosquitoes of N. America receive mention. The Simuliidae, Tabanidae and Muscidae, especially those of importance in N. America, are described. Considerable attention is given to lice and fleas and their control, and a few pages are devoted to the bed bug.

Finally there is a short section on parasiticides and a longer one on technique.

The general tone of the book is dogmatic, as it should be to fulfil the purpose for which it was written. It is clear and precise, with but little discussion of debatable points, and is accurate. The illustrations are excellent throughout. The order in which the various parasites are dealt with is not always the order in which they are classed scientifically. This may not be of great importance, but to the reviewer it seems probable that tables giving the scientific arrangement of the parasites by Phylum, Class, Order and so on, with brief descriptions of the points of similarity or difference between the different generic groups, would make for clarity in the mind of a student. Otherwise the book is excellent for its purpose and can be confidently recommended for class work. *C. W.*

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